SURGERY
GYNECOLOGY AND OBSTETRICS

VOLUME 83 JULY, 1946 NUMBER 1

LOCAL CHEMOTHERAPY OF WOUNDS

Tissue Toxicity of Certain Antibacterial Substances

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IN this investigation the tissue toxicity of some of the newer antibacterial substances is compared with their speed of action and fate in the tissues. The substances tested were streptomycin, sulfamylon[1], calcium penicillin, parachlorophenol, tyrothricin, and zephiran.[2] The results of local chemotherapy with two of the antibacterial substances of low toxicity and rapid bacteriocidal action will be presented.

The antibacterial substances were tested for toxicity against cells growing in tissue culture, for the amount of irritation caused to the conjunctiva of the eye, for their capacity to damage subcutaneous blood vessels, for their capacity to destroy muscle on injection, to cause peritoneal adhesions, and to influence the rate of wound healing. Their antibacterial activity was tested in the presence of blood against the common bacteria found in the flora of wounds.

TISSUE CULTURE TESTS

The tissue culture tests demonstrated the concentration which was toxic when constantly in contact with cells. The method employed has previously been described by Simms (12). Its advantage is that the results were obtained against adult cells which possess growth requirements differing from embryonal cells.

Epithelial cells and fibroblasts from adult animals were incubated in serum ultrafiltrate for 24 hours to keep them alive and they were then transposed to chicken plasma to grow. Some were grown directly in plasma. The substances to be investigated were added in minute amounts either to the serum ultrafiltrate or the plasma as indicated in Table I. If the substance was toxic, none of the cells grew or grew very poorly. If the substance was partially toxic, the growth of the cells was poor.

Results of tissue culture tests. Bacteriocidal amounts of most of the known antiseptics killed cells. The complete data on these tests will be reported elsewhere by Simms and Parsley (11). Calcium penicillin, 100 units per cubic centimeter, was inert. Bacteriocidal concentrations of streptomycin and sulfamylon were only mildly inhibitory to cells. Streptomycin, 100 units per cubic centimeter, was inert, while 200 units were only moderately inhibitory.

Previously, streptothricin was found to be slightly more toxic; 100 units being slightly inhibitory, while 200 units were definitely toxic.

Sulfamylon, 0.15 per cent, was only moderately inhibitory while 0.1 per cent was toxic. On the other hand, zephiran (.01%), parachlorophenol (.001%), and tyrothricin (.05%) were toxic to cells.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University. Tissue culture work was done by Dr. Henry Simms, Ph.D., and Dr. Mary Parsley, Ph.D.; technical assistance furnished by Janice Kleinsorge and Joan Kennedy.

[1] 4-amino, 2-methyl benzene sulfonamide hydrochloride = Marfanil = homosulfanilamide = Mesudin.

[2] Benyl triakyl ammonium chloride.

TABLE I.

Substances	Stimulating	Inert	Inhibitory	Toxic
Sulfamylon in $\frac{UF}{3}$			.05%–A 40	0.1%–A 0
in $\frac{Pl}{3}$			.05%–F 44	
			.01%–E 40	
Streptomycin		.02% (100 u)/ml	.02% (200 u)/ml	
Streptothricin			.02% (200 u)/ml	.02% (200 u)/ml
			A 37	A 1
Tyrothricin				.05%
Parachlorophenol				.01% E, F 0
				.001% A 0
Calcium penicillin in $\frac{UF}{3}$		.03% (100 u)/ml		
		A 90		
		.003% (100 u)/ml		
		A 120 E 117		
in Pl			.03% (100 u)/ml	
Zephiran				.02% A 0
				.01% A 0
Sulfadiazine in $\frac{UF}{10}$	.085% A 175			
	.05% A 131			
in $\frac{X}{0}$			.085% A 56	
			.05% A 53	
			.005% A 71	

Key

UF = serum ultrafiltrate
Pl = plasma
X0 = a special physiological solution
u = units

A = aorta fibroblasts
E = epithelial cells
F = fibroblasts
O = no growth, over 125 stimulating, 125 to 75 = inert, 75 to 25 inhibitory, 25 to 0 = toxic

Thus zephiran, parachlorophenol, and tyrothricin, in the dilutions employed to inhibit the growth of bacteria, were toxic to cells when constantly in contact with them. Penicillin was inert while streptomycin and sulfamylon mildly inhibited the growth of cells.

EYE TESTS

The eye tests indicated the concentration of agent which would be irritating to the delicate tissues of the conjunctiva. Vasodilatation, edema, and exudate are produced if the substances are irritating. Contact with the tissues is short in this test and there is considerable dilution but the tissues are very sensitive.

Two or three drops of the solution to be tested (Table II for concentrations) were placed in the eye of a rabbit and a similar amount of saline in the opposite eye. The immediate reaction of blood vessels was noted together with their condition 30 minutes later. Twenty-four hours afterward, the state of the blood vessels and the amount of edema were observed.

Results of eye tests. The results are shown in Table II. At their antibacterial concentrations nearly all the substances and sometimes even the saline caused some immediate injection of the blood vessels. Parachlorophenol (0.25%) caused more immediate redness than the other agents. At the end of one-half hour most of the treated conjunctivae had returned to their normal appearance, while those treated with calcium penicillin (200 units per c.c.), tyrothricin (0.05%) and parachlorophenol (0.25%) still showed slight redness. After 24 hours no abnormal reactions were observed with any of the antibacterial agents, indicating that except for causing a transitory reaction, none of them really injures the conjunctiva of the eye.

MUSCLE INJECTIONS

The injections in muscle indicated the capacity of the agent to cause an inflammatory reaction and fibrosis in muscle—the period of contact with the tissues was the interval between the time of injection and the absorption or neutralization of the agent.

Five to 10 cubic centimeters of the various antibacterial substances was injected in the muscles of the leg of the rabbit. To eliminate error in locating the site later, the needle was inserted anteriorly to the bone of the hind leg at a definite distance above the knee joint. In the opposite leg, the same amount of saline was injected. Twenty-four hours and 48 hours later the animals were killed and the tissues were examined grossly and microscopically. In order to be certain of the identification of the injected site in the animals living for 4 days and 1 week, a long incision was made under aseptic precaution through the skin of the back. The points of injection were marked with silk

TABLE II.—EYE TESTS—5 DROPS EACH EYE

Date	Substance	Immediate reaction	½ hour	Reaction after 24 hours
10–20–45	Ca penicillin 200 u. per c.c.	Slight blanching	Very slightly red	Normal
0– 1–45	Streptomycin 200 u. per c.c.	Very slight reddening	Normal	Normal
0– 1–45	Sulfamylon 5%	Very slight reddening	Normal	Normal
0– 1–45	Streptomycin and sulfamylon mixture[1]	No change	Very slight redness	Normal
10– 1–45	.05% Tyrothricin	Very slight redness	Still slightly red	Normal
10– 1–45	.25% p.chlorophenol	Marked redness	Very slightly red	Normal
10– 2–45	.5% p.chlorophenol	Whole eye very red	Normal	Normal
Typical reaction in all rabbits	Saline	No reaction or very slight redness	Normal	Normal

[1]Consisted of 200 units of streptomycin per c.c., 5 per cent of sulfamylon, and ½ per cent of sodium benzoate.

ligatures in the fascia overlying the back muscle. Then the skin was resutured. The tissue immediately beneath the sutures was subsequently removed for biopsy.

Results of muscle injections. The results are shown in Table III. Zephiran produced edema, leucocytosis, and deposition of fibrin for the first 48 hours, and after 96 hours streaks of mononuclear cells could be found. Tyrothricin produced exudation and edema and finally fibrosis. Calcium penicillin produced some slight edema and exudation for the first 24 hours although thereafter no tissue reaction was observed. Streptomycin and sulfamylon produced a reaction comparable to calcium penicillin. A mixture of streptomycin and sulfamylon with sodium benzoate produced no more edema or leucocytosis than the single substances. Parachlorophenol produced a slight amount of edema and infiltration for 24 hours. After 48 hours the myosin seemed coagulated and after 1 week degenerated muscle and attempts at regeneration were seen. There was considerable fibrosis. Saline occasionally produced a slight exudation after 24 hours. Phenol and iodine, which were used for basis of comparison, produced frank necrosis and suppuration.

In summary, tyrothricin, zephiran, and parachlorophenol produced considerable tissue reaction and fibrosis while streptomycin and sulfamylon, calcium penicillin produced tissue reactions of such low grade that parenteral administration of these substances would be tolerated.

INSTILLATION IN PERITONEAL CAVITY

Only the substances which produced minimal tissue reactions were injected into the peritoneal cavity. Twenty cubic centimeters of calcium penicillin, sulfamylon, streptomycin, and the combination of the last two with sodium benzoate, were injected into the peritoneal cavity of the rabbit. Ten days later the peritoneal cavity was examined and was found to be free of adhesions.

DESIRABLE ANTIBACTERIAL PROPERTIES FOR LOCAL CHEMOTHERAPY

For local chemotherapy antibacterial substances should possess prompt bacteriocidal activity in the presence of blood. Regardless of how soluble the antibacterial substance might be, the portion of it in solution is the important component. It affects the growth of the bacteria and causes the inflammatory reactions. This portion is either quickly absorbed or neutralized while the insoluble residue is treated as a foreign body. When neutralized, this fraction loses its antibacterial properties. The portion in solution may be adsorbed temporarily on the tissue, yet thereafter rapid absorption occurs unless it has sufficient toxicity to produce an edema. Then, however, neutralization occurs.

The insoluble residue of the antibacterial substance is encapsulated by a foreign body reaction. This process of encapsulation is distorted and delayed in direct proportion to the amount of inflammatory reaction produced by the portion in solution.

TABLE III.—RESULTS OF INJECTION INTO MUSCLE

Substance	Microscopic appearance			
	After 24 hours	After 48 hours	After 96 hours	After 1 week
Calcium penicillin 200 u. per c.c.	Slight edema and a considerable number of leucocytes	No change.	No change.	No change
Sulfamylon 5%	Occasional leucocytes. Minimal reaction. Fibrin deposits	Very slight change. Coagulation of muscle substance into irregular small pink globules. A few more leucocytes than in ordinary muscle	Slight infiltration of round cells	No change
Streptomycin	Some leucocytes. Slight edema	Nothing to distinguish it from saline. Some leucocytes	Very tiny area of new granulations between muscle fibers	No change
Streptomycin 200 u. per c.c. Sulfamylon 5% Sodium benzoate 1.2%	No evidence of injection	No change	No tissue reaction	No change
Zephiran 1:1000	Marked edema and infiltration of leucocytes. Fibrin	Some edema and a number of leucocytes. Fibrin	Streak of mononuclear cells	
Tyrothricin .05%	Marked edema and a considerable number of leucocytes. Fibrin	Edema and a few leucocytes. Muscle looks coagulated	Considerable destruction of muscle with replacement by fibroblasts, mononuclear and capillaries. Occasional giant cells and nest of leucocytes	Fibrosis. Giant cells. Degeneration of muscle
Para-hydroxyphenol .25%	Edema and some leucocytes. Considerable fibrin	Some leucocytes. Muscle looks coagulated	Streak of muscle coagulated	Fibrosis. Many mononuclear cells. Marked degeneration of muscle
Iodine 3.5%			Muscles are coagulated and necrotic. Gross destruction of muscle	
Phenol 1%			Extensive destruction of muscle with fibroblasts, granulation and round cell infiltration	
Sulfamylon 5%		Slightly more infiltration of round cells. Very slight change in muscle substance		
Normal saline	Minimal reaction	Some infiltration of round cells	Small area of separation of muscle fibers with many fibroblasts and young granulations	No change

Conversely, because of the rapidity of absorption and neutralization of the portion in solution, antibacterial agents which possess only bacteriostatic activity and therefore require considerable time to act, are not useful for local chemotherapy unless the soluble portion can remain adsorbed for a long time without neutralization, or the parent substance dissolves slowly, or a base is employed slowly to release the soluble portion. The last two possibilities usually lead to continuing inflammatory reaction and fibrosis and what is more common, extrusion of the offending substance.

BACTERIOLOGICAL TESTS

To find out how a short contact with the antibacterial substances would kill bacteria, the filter paper, blood agar plate method of testing antiseptics, was adapted for our purposes (2). A 24 hour culture of the particular bacteria to be investigated was streaked on a blood agar plate and the plate was incubated for 3 hours. Then a piece of filter paper dipped in a solution of the antibacterial substance was placed on the agar for 10 minutes. Ten minutes was selected because this length of time is seldom exceeded in carrying out local chemotherapy. The control area was treated with saline or not at all. The plate was then incubated for 24 hours.

Bacteria grew abundantly over the control areas and over the rest of the plate where there was no antibacterial substance, but not in the area of contact with the filter paper containing the antibacterial substance. This area remained clear. Considering that bacteria were smeared over the entire surface of the plate and that they were either growing or were

TABLE IV.—SULFAMYLON 5 PER CENT—10 MINUTE CONTACT

Date of test	Strain of bacteria	Inhibition of growth in area contacted by paper	Inhibition zone about this area
5-17-45	Staphylococcus (coagulase positive)	++++	+
5-29-45	Staphylococcus (coagulase positive)	++++	+
6-12-45	Staphylococcus (coagulase positive)	++++	++
6-12-45	Staphylococcus (coagulase positive)	++++	++
6-22-45	Staphylococcus (coagulase positive)	++++	++++
8-14-45	Bacillus coli	++++	++++
8-14-45	Bacillus proteus	++++	+
8-14-45	Bacillus pyocyaneus	++++	o
8-14-45	Bacillus pyocyaneus	+++*	o
10-10-45	Hemolytic streptococcus	++++	o
10-10-45	Green streptococcus	++++	++

*Overgrowing colonies after 24 hours.

TABLE V.—STREPTOMYCIN 200 UNITS PER CUBIC CENTIMETER 10 MINUTE CONTACT

Date of test	Strain of bacteria	Inhibition of growth of bacteria in area contacted by paper	Inhibition zone about this area
5-17-45	Bacillus coli	++++	++
6-12-45	Bacillus coli	++++	++
6-22-45	Bacillus coli	++++	+
6-13-45	Bacillus proteus	++++	+
6-22-45	Bacillus proteus	++++	+
5-17-45	Bacillus proteus	++++	++++
6-12-45	Staphylococcus (coagulase positive)	++++	++
6-22-45	Staphylococcus (coagulase positive)	++++	++++
6-12-45	Bacillus pyocyaneus	+++*	o
6-22-45	Bacillus pyocyaneus	+++*	o
5-17-45	Bacillus pyocyaneus	++‡	o
10-10-45	Streptococcus hemolyticus	o	o
10-10-45	Green streptococcus	o	o

*Spread in from edges.
‡Overgrown in 36 hours.

kept alive by incubating their failure to develop further in the area of contact with the agent indicated that the substance was definitely bacteriocidal. If the antibacterial substance caused hemolysis of blood this property could also be detected by the method.

About the area where the filter paper was placed there also occurred a clear zone where the bacteria did not grow. This zone varied in extent with the degree of bacteriocidal activity of the substance tested, with the sensitivity of the bacteria to the antibacterial substance and with the capacity of the antibacterial substance to diffuse through the agar.

The sensitivity of penicillin and streptomycin to acidity and dilution has been demonstrated (13, 10). Streptomycin has its optimal antibacterial activity at *p*H 7.8 and changes to the acid side detract from this activity. It is completely destroyed at *p*H 2 as is penicillin. No such information is available for sulfamylon. Hence these points were determined by the method employed.

Results. The results which are to be described are for the conditions of the experiment and should not be interpreted for different concentrations or longer contacts with the bacteria.

Sulfamylon (5%) killed staphylococci, the hemolytic and green streptococci, Pseudomonas aeruginosa, Escherichia coli, and proteus (Table IV). With all these bacteria therewas a zone of inhibition about the area of contact with the paper except with the hemolytic streptococcus and pyocyaneus (Pseudomonas aeruginosa). Pyocyaneus was killed only within the area of contact with the paper and quickly grew in again from the edges over the cleared area.

After a similar period of contact, streptomycin, 200 units per cubic centimeter (Table V), killed the staphylococcus, pyocyaneus, Escherichia coli and proteus. Pyocyaneus again grew back over the cleared area and more rapidly than with sulfamylon. Streptomycin was ineffective against the strains of hemolytic and the green streptococci employed. There was luxuriant growth in the area of contact with the paper.

Originally, the hypothesis was entertained that sulfamylon and streptomycin should be combined on the thesis that the former would destroy gram positive bacteria while the latter would destroy the gram negative ones. Actually when used in this manner both seem to have about the same range of bacteriocidal activity except for the streptococci. Both streptomycin and sulfamylon killed strains of staphylococci, the Escherichia coli, and pro-

TABLE VI.—STREPTOMYCIN 200 UNITS PER CUBIC CENTIMETER AND SULFAMYLON 5 PER CENT AND 0.5 PER CENT SODIUM BENZOATE

Date of test	Strain of bacteria	Inhibition of growth of bacteria in area contacted by paper	Inhibition zone about this area
5–25–45	Staphylococcus	++++	++
6–12–45	Staphylococcus	++++	++++
6–12–45	Staphylococcus	++++	++++
6–1–45	Staphylococcus	++++	++
6–1–45	Staphylococcus	++++	++
5–17–45	Staphylococcus and Bacillus coli	++++	++
6–12–45	Bacillus coli	++++	++
6–24–45	Bacillus coli	++++	++
6–13–45	Bacillus proteus	++++	+–
6–22–45	Bacillus proteus	++++	+
6–12–45	Bacillus pyocyaneus	++++	+
6–22–45	Bacillus pyocyaneus	++++	+
10–10–45	Streptococcus hemolyticus	++++	+++
10–10–45	Green streptococcus	++++	+

TABLE VII.—CALCIUM PENICILLIN 200 UNITS PER CUBIC CENTIMETER—10 MINUTE CONTACT

Date of test	Strain of bacteria	Inhibition of growth of bacteria in area contacted by paper	Inhibition zone about this area
5–21–45	Staphylococcus (penicillin resistant strain)	+	0
5–24–45	Staphylococcus	++++	+++++
6–1–45	Staphylococcus	++++	++++
6–1–45	Staphylococcus (penicillin resistant strain)	0	0
8–14–45	Bacillus coli	0	0
8–14–45	Bacillus proteus	±	0
8–14–45	Bacillus pyocyaneus	0	0
8–14–45	Bacillus pyocyaneus	0	0

teus. They killed Pseudomonas aeruginosa, and they both allowed regrowth of this bacteria. Against the streptococci, sulfamylon (5%) was efficient while streptomycin, 200 units per cubic centimeter, was not. The need to use large amounts of streptomycin to destroy the streptococcus has been shown both by Waksman and the bacteriologists at Merck (13). Both drugs had a wider range of bacteriocidal activity than did penicillin.

The combination of streptomycin, 200 units per cubic centimeter, and sulfamylon 5 per cent, destroyed all strains of bacteria encountered and was slightly more effective against pyocyaneus (Table VI). Thirty different strains of bacteria were tested against the combination without finding a resistant one. Besides four mixed cultures recovered from patients which were not affected by penicillin were destroyed by the combination of sulfamylon and streptomycin.

The zones of inhibition about the area of contact with the paper were wider with the combination of agents than with either antibacterial substance alone. They were narrower, however, with pyocyaneus and with the green streptococcus than with any of the other bacteria and if the cultures stood longer than 24 hours pyocyaneus began to grow back again over the cleared zone.

Calcium penicillin, 200 units per cubic centimeter, was very effective in destroying the hemolytic streptococci and most strains of staphylococci. On the other hand, Escherichia coli, proteus and pyocyaneus were unharmed (Table VII). Two penicillin-resistant strains of staphylococci are included. They were not killed although the mixture of streptomycin and sulfamylon quickly destroyed them.

The tests also showed that like penicillin, streptomycin and sulfamylon acted quickly, whereas sodium sulfadiazine did not destroy the bacteria in the period of contact, (Fig. 1).

Parachlorophenol (0.25%) inhibited the growth of pyocyaneus, the staphylococcus and a mixture of staphylococcus and pyocyaneus. It did not completely inhibit the growth of proteus, nor the green streptococcus. It was ineffective against the hemolytic streptococcus (Table VIII).

Zephiran 1:1000 was more effective against the gram positive bacteria but was relatively ineffective against pyocyaneus and proteus. Bacillus coli was not completely inhibited (Table VIII).

Tyrothricin (0.05%) destroyed gram positive bacteria but was ineffective against pyocyaneus and proteus. Bacillus coli was not affected (Table VIII).

The results for the effects of changes in acidity and dilution on sulfamylon are recorded in Tables IX and X.

Comment on bacteriological test. Although the filter paper was in contact with the blood agar plate and the bacteria for 10 minutes, actually the antibacterial substance was absorbed into the agar and it was in contact with the bacteria for a much longer period of time. How long a contact is required to kill bacteria is difficult to state for the answer depends in part on the number of bacteria present and whether they are in the lag or growth phase of their development. Tests of the phenol coefficient type showed that penicillin was capable of destroying many more bacteria than either streptomycin or sulfamylon when the bacteria were sensitive to its action. Yet, a definite period of time was required for penicillin to act. For example, when penicillinase was added to a mixture of bacteria and penicillin, 4 hours' contact was found to be the period required for the penicillin to kill the bacteria. Similar substances are not available to determine the duration of contact necessary for the other antibacterial substances to act.

Clinically, no resistant bacteria should be encountered. These tests are important, therefore, only because they show that more strains of bacteria are susceptible to action of streptomycin and sulfamylon than to penicillin and that the combination of the two encounters very few resistant strains. Combinations with penicillin should be tested for their capacity to destroy various strains of bacteria.

Obviously, sulfamylon is the only drug which continues to be effective with markedly increased acidity. The change of susceptibility of Escherichia coli is of interest (Table X).

Influence on rate of wound healing. These tests studied the influence of the antibacterial substance on the character and length of the exudative phase of healing of the open wound and on the rate of regeneration of new tissue. The conditions which the antibacterial substance encounters on the open wound are very complex. In the open wound there is dilution of the agent by the secretions of the wound and there is constant absorption of the antibacterial substance from the surface of the wound

Fig. 1. a. Sodium sulfadiazine. b. Streptomycin. c. Sulfamylon plus streptomycin.

especially after granulations have formed. For these reasons much higher concentrations can be employed, or to state the situation conversely, granulations are not as easily damaged by antibacterial agents as are fresh tissues. Further because of the absorption, the antibacterial agents must be supplied to the wound in a base which acts as a reservoir for the material. This base must not only be innocuous but it must maintain the proper physical state of the tissues. To answer these requirements cholesterized petrolatum was employed for the experiment though only about 2 per cent of the original content of antibacterial substance seeps from this base. On the other hand, the cells are continuously in contact with this amount of the active agent as in the tissue culture method of testing.

The open wound was made on the rabbit's ear leaving a small island of skin in the center. It was photographed every day. The character of the exudate, of the granulations, the time when the island began to grow, and the rate of its growth were observed.

The results are shown in Table XI.

These animals were killed at the end of an experiment to determine if absorption of the antibacterial substance from the wound caused damage to the excretory and neutralizing tis-

TABLE VIII.—OTHER ANTISEPTIC AGENTS—10 MINUTE CONTACT

Agent	Date of Test	Strain of bacteria	Inhibition of growth of bacteria in area contacted by paper	Inhibition zone about this area
Sodium sulfadiazine 5/10%	6– 6–45	Staphylococcus	⊕	⊕
Sodium sulfadiazine 5/10%	6–12–45	Staphylococcus	++	⊕
Tyrothricin (.05%)	10–26–45	Green streptococcus	++++	++
Iodine (3.2%)	6– 6–45	Staphylococcus	++++	++
Phenol (2%)	6–12–45	Staphylococcus	++*	○
Phenol (2%)	5–17–45	Bacillus coli	++++	+
Phenol (2%)	6–13–45	Bacillus proteus	++	○
Phenol (2%)	6–12–45	Bacillus pyocyaneus	++++	○
Tyrothricin (.05%)	6– 1–45	Staphylococcus	++++	++
Tyrothricin (.05%)	8–18–45	Bacillus pyocyaneus	○	⊕
Tyrothricin (.05%)	10–26–45	Hemolytic streptococcus	++	○
Tyrothricin (.05%)	10–26–45	Bacillus coli	○	○
Tyrothricin (.05%)	10–26–45	Bacillus proteus	○	⊕
Tyrothricin (.05%)	10–26–45	Green streptococcus	++++	++
Zephiran 1:1000	3–22–45	Staphylococcus	++++	+‡
Zephiran 1:1000	8–18–45	Bacillus pyocyaneus	+†	○‡
Zephiran 1:1000	8–18–45	Bacillus coli	+++	—‡
Zephiran 1:1000	8–18–45	Bacillus proteus	+	—‡
Zephiran 1:1000	10–26–45	Hemolytic streptococcus	++++	+‡
Zephiran 1:1000	10–26–45	Green streptococcus	++++	++‡
P chlorophenol (.25%)	10–26–45	Bacillus proteus	++	—
P chlorophenol (.25%)	5–15–45	Staphylococcus and pyocyaneus	++++	—
P chlorophenol (.25%)	5–15–45	Bacillus pyocyaneus	++++	+
P chlorophenol (.25%)	5–25–45	Staphylococcus	++++	○
P chlorophenol (.25%)	10–21–45	Green streptococcus	++	○
P chlorophenol (.25%)	10–26–45	Hemolytic streptococcus	○	○

*Overgrowth from edges
†Few colonies
‡Slight hemolysis

sues, such as the liver and kidney. Specimens were taken for biopsy.

RATE OF WOUND HEALING

Results. The average index obtained was 7.5 days, i.e., for the length of time required for the exudative phase and to produce 2 millimeters of new tissue. The best rate ever obtained was 5.6 days. As can be seen from the Table XI, 400 units of streptomycin combined with 5 per cent sulfamylon definitely slowed the rate of healing. Parachlorophenol gave only a fair rate and tyrothricin was just average and produced a slight exudate. Granulations remained thin with it. On the other hand, excellent healing rates were obtained with sulfamylon, 5 per cent and 1 per cent, and streptomycin, 200 units per cubic centimeter, and with the combination of these. Calcium penicillin gave only an average healing rate while sodium penicillin definitely retarded the rate of healing.

Discussion. A pattern is presented for investigating the merits of chemotherapeutic substances to use locally.

Tests will ultimately have to be conducted to determine the concentration of penicillin, sulfamylon, and streptomycin which will cause tissue reactions. Then the antibacterial activity of a slightly weaker solution will have to be studied. For example, 300 units per cubic centimeter of streptomycin or an amount

TABLE IX.—THE EFFECT OF DILUTION ON ANTIBACTERIAL ACTIVITY OF SULFAMYLON

Date	Strain of bacteria	Inhibition in area of contact	Inhibition zone about this area
		Sulfamylon .05%	
9–25	Staphylococcus (coagulase positive)	0	0
9–25	Bacillus coli	0	0
		Sulfamylon .1%	
9–25	Staphylococcus (coagulase positive)	0	0
9–25	Bacillus coli	0	0
		Sulfamylon 1%	
9–25	Staphylococcus (coagulase positive)	+ +	0
9–25	Bacillus coli	0	0
		Sulfamylon 2%	
10–1	Staphylococcus (coagulase positive)	+ + + +	+ +
10–4	Staphylococcus (coagulase positive)	+ + + +	+
10–1	Bacillus coli	+ + +	0
10–4	Bacillus coli	0	0
		Sulfamylon 5%	
10–1	Staphylococcus (coagulase positive)	+ + + +	+ + +
10–4	Staphylococcus (coagulase positive)	+ + + +	+
10–1	Bacillus coli	+ + + +	+ + +
10–4	Bacillus coli	+ +	0
		Sulfamylon 4%	
10–1	Staphylococcus (coagulase positive)	+ + + +	+ + + +
10–4	Staphylococcus (coagulase positive)	+ + + +	+ + + +
10–1	Bacillus coli	+ +	0
10–4	Bacillus coli	+ + + +	+ + + +

between the nontoxic 200 units per cubic centimeter and the toxic 400 units per cubic centimeter should be tried. In fairness also, it should be said that streptomycin is still in the early stages of development and products of increased purity and less tissue toxicity will undoubtedly be produced. These purified samples will have to be tested. Several reports (3, 9, 10), have been made that massive doses of penicillin produced inflammatory changes and tissue necrosis locally, but the dilution employed was not mentioned. Medewar reported that crude penicillin (kind not mentioned) in a dilution of 1:1600 was toxic to fibroblasts after 48 hours. Herrell and Heilman found that above 500 micrograms per cubic centimeter penicillin showed cytotoxicity for lymphocytes. In other words, there is a concentration where penicillin becomes toxic. The strongest concentration of sulfamylon which will cause tissue reaction is not even suspected. Sulfamylon hydrochloride solution 5 per cent used in these experiments had a *p*H of approximately 5.2 and this acidity can be neutralized without loss of antibacterial power. Theoretically, the neutralized solution should be less toxic also.

Historically, many antibacterial substances have failed as local chemotherapeutic agents because the complete pattern of requirements has not been met, *i.e.*, they were toxic or they did not act quickly in the presence of blood and pus or they were readily influenced by other changes in the environment. For example, iodine and mercuric chloride possessed none of the necessary characteristics except the capacity to destroy bacteria. More recently the sulfonamides failed because all were slow to act and were inhibited by para-aminobenzoic acid. Moreover, when used as pow-

TABLE X.—THE EFFECT OF *p*H. ON ANTIBACTERIAL ACTIVITY OF 5% SULFAMYLON

Date	Strain of bacteria	Inhibition in area of contact	Inhibition zone about this area
		*p*H. 5.1	
10–5	Staphylococcus (coagulase positive)	++++	+
10–8	Staphylococcus (coagulase positive)	++++	o
10–5	Bacillus coli	o	o
10–8	Pyocyaneus	++++ overgrowth in 48 hours	+++ overgrowth in 48 hours
10–5	Pyocyaneus	++++ overgrowth in 36 hours	++++ overgrowth in 36 hours
		*p*H. 3.8	
10–5	Staphylococcus (coagulase positive)	++++	++++
10–8	Staphylococcus (coagulase positive)	++++	+++
10–5	Bacillus coli	o	o
10–5	Pyocyaneus	++++ overgrowth in 36 hours	o
10–8	Pyocyaneus	++++ overgrowth in 48 hours	+++ overgrowth in 48 hours
		*p*H. 2.0	
10–5	Staphylococcus (coagulase positive)	++++	++++
10–8	Staphylococcus (coagulase positive)	++++	+++
10–5	Bacillus coli	o	o
10–5	Pyocyaneus	++++ overgrowth in 36 hours	+++ overgrowth in 36 hours
10–8	Pyocyaneus	++++ overgrowth in 36 hours	+++ overgrowth in 36 hours

ders, as they were, the more soluble sulfanilamide was toxic while the less soluble sulfathiazole and sulfadiazine, remained as foreign bodies which were ultimately extruded from the tissues. All sulfonamides caused some reinitiation of bleeding in the wound, a property which sulfamylon possesses only to a minor degree. Some slight bleeding was observed in one instance when a very large quantity of the 5 per cent solution of sulfamylon was put into a peritoneal cavity studded with tubercles.

Penicillin has been used locally to treat staphylococcus and streptococcus skin infections and for instillations into empyema cavities. For local skin diseases penicillin is usually applied in the form of an ointment. Dry calcium penicillin powder is irritating to the surfaces of fresh wounds. Sodium penicillin is more irritating than calcium and even 200 to 500 units per cubic centimeter in saline causes a burning sensation when applied locally. No cases could be found in which clean contaminated wounds were flushed with a saline suspension of penicillin to prevent infection before suturing. There is no reason why the solution of penicillin nor it combined with streptomycin or neutralized sulfamylon should not be added to the irrigating fluid used in débridement to increase the antibacterial range of that fluid. Dry penicillin powder has been placed in wounds to be sutured and in open wounds. Those which are to be left open, especially those with granulation, tolerate dry penicillin well but dry powders of any of antibacterial substances, even when they exhibit low toxicity, should not be used in wounds which are to be sutured. A saturated solution results which may be toxic as the work with penicillin suggests (5, 3, 10), and besides saturated solutions are not needed for antibacterial action.

Although penicillin has been repeatedly injected in lesser concentrations into muscle for parenteral administration, injections of a solution of it about an area for the prevention or treatment of an infection has not been practiced. In the frankly infected wound, penicillin is not effective because of the excessive

amounts of dead tissue present, and penicillin is destroyed in the presence of gram negative bacteria. The prediction can be made also that streptomycin and sulfamylon will not be successful in the local treatment of the purulent wound even though both substances have wider range of antibacterial activity than does penicillin. Local chemotherapy will not be successful in the presence of slough until there is also a chemotherapy of slough. Yet, the published reports on the local use of sulfamylon are optimistic.

Nearly all bacteriologists who have worked with sulfamylon have proposed that the drug should be used for local treatment of wounds, but only Mitchell, Reese, and Robinson have published their results. They applied powdered sulfamylon to 22 purulent wounds including 4 burns. In one-third of the cases, no growth could be obtained on cultures after 4 to 12 days' treatment, and 70 per cent showed improvement. The German Army apparently made extensive use of sulfamylon for the local treatment of wounds, but their records are not available.

In experimental animals, Hamre, Walker, Durham, Van Dyke, and Rake showed that sulfamylon is one of the most effective agents for the local treatment of gas gangrene although they used comparatively small amounts of the drug. They recommended a clinical trial of local treatment and also noted that its acute and chronic toxicity was of low order. The *in vitro* activity of sulfamylon against the anaerobic gas forming micro-organisms has been confirmed by others (9, 14). There is universal agreement in the literature that sulfamylon is not inhibited by para-amino benzoic acid (1, 8) and that unlike penicillin it is not destroyed by penicillinase.

These experiments also demonstrated that changes in the acidity of the wound would not destroy the activity of sulfamylon except against Escherichia coli. Locally, a concentration of 3 per cent or greater must be maintained.

The local use of streptomycin is reported for the first time in this publication. It was used in combination with sulfamylon. Sutured wounds and certain types of open wounds were successfully treated. On the other hand, local applications of the combination, like penicillin, were not too successful in ridding the open wound of infection. Why the combination was successful in certain types of wounds and not in others had best be explained.

TABLE XI.—INDEX OF WOUND HEALING*

Animal No.	Amount in cholesterized petrolatum	Index	Remarks
569	1% sulfamylon	6.8	Excellent healing
573	5% sulfamylon	6.9	Excellent healing
571	200u. streptomycin, 5% sulfamylon applied daily to wound. Overlaid with calcium penicillin	7.3	Excellent healing
577	5% sulfamylon + 200u. streptomycin	5.7	Excellent healing
574	5% sulfamylon + 400u. streptomycin	10	Scum-like exudate. No growth on island of epithelium. Granulations are thin.
565	Penicillin 200u. per c.c.	7.0	Excellent healing
566	Streptomycin 200u. per c.c.	6.4	Excellent healing
422	1% zephiran 1:2000	6.6	Excellent healing
430	2% zephiran 1:2000	6.8	Excellent healing
440	Tyrothricin 0.05%	7.0	Average healing produced some exudate
584	Parachlorophenol 0.25%	7.9	Fair healing
415	Sulfadiazine 1%	6.3	Excellent healing

*Index = days required for exudative phase plus days required to produce 2 millimeters of new epithelium. Average index = 7.5. Best rate ever obtained = 5.6 days.

Local chemotherapy of the open wound is a more complex problem than chemotherapy of the sutured wound. Some of the difficulties encountered in treatment of the open wound have been pointed out already. Besides the open wound is recontaminated with bacteria at every dressing, the bacterial flora changes and the bacteria develop fastness for the chemotherapeutic agent. Then slough must be liquefied for slough is a nutrient and protector of the bacteria. On the other hand, in the sutured wound the bacterial contamination is complete at the time of suturing. The tissues are freshly injured and easily injured again by the agent. The chemotherapeutic agent can be used once only at the time of closure of the wound.

Among open wounds and inflammatory conditions which were free of slough, 68 wounds, burns, and rectal conditions were treated with the solution of sulfamylon and streptomycin. Satisfactory results were obtained without

signs of toxicity or other untoward reactions but pyocyaneus quickly returned to the large open wounds and to the larger burns. The solution of the combination, locally applied, was not successful in eliminating bacteria from wounds containing bone sequestra and extensive slough.

On the other hand, local chemotherapy of the sutured wound with streptomycin and sulfamylon was very successful in the small number of cases tried. Thirty clean, contaminated, sutured wounds washed with the solution healed *per primam*. In fact, soft white healing was obtained in each one. These wounds were usually contaminated at operation by opening into the large bowel. The line of anastomosis in the colon, for example, was sponged with the solution of streptomycin and sulfamylon, and, after closure of the peritoneum, the wound was irrigated with it. Some of these cases were distinctly of the type which usually develop infection, and the results are viewed with considerable optimism. Two case histories, one of an abdominal perineal resection for carcinoma in a patient with impending cardiac failure with an extremely thick panniculus and the other of a biopsy of infected buboes, are appended. The efficacy of the local use of the combination in contaminated wounds which can be sutured will need statistical evaluation to prove its worth. At least, however, a sufficient number of cases have been done to demonstrate that induration and discharge of serum which complicated the early chemotherapy of sutured wounds with the sulfonamides will not be encountered and the combination clinically does not interfere with healing.

Hunter described the properties of the ideal subcutaneous antiseptic as follows: "High germicidal or inhibitory properties, no toxicity or at least low toxicity, freedom from specificity, efficiency in the presence of organic material, power to penetrate, stability and perhaps other characteristics including low cost." The water solution of streptomycin, 200 units per cubic centimeter, and sulfamylon 5 per cent approaches this description. The results obtained to date with this mixture in the treatment of sutured wounds both in animals and in the patients suggests that the combination of agents might well prove to be both the ideal subcutaneous antiseptic and ideal local chemotherapeutic agent for the sutured wound. The combination of sulfamylon and streptomycin supports the growth of molds when it stands in the laboratory.

The other antibacterial agents tested, tyrothricin, parachlorophenol, and zephiran have a toxicity which permits their use on granulating wounds only. Herrell and Heilman could not find that tyrothricin was extremely toxic to lymphocytes present in tissue cultures. On the other hand, Waksman claims that tyrothricin is toxic. Tyrothricin and zephiran and parachlorophenol have been used, apparently with success, to treat sluggish granulating wounds such as leg ulcers. There are no reports of their employment as subcutaneous antiseptics.

CLINICAL CASES

CASE I. Female, aged 60 years. Patient was an extremely obese hypertensive patient with one-half flight dyspnea and enlarged heart. A diagnosis of carcinoma of the rectum was proved by biopsy. Patient was an extremely poor operative risk. Operation consisted of combined abdominoperineal resection. Closure of the left lower rectus splitting incision was accomplished with interrupted silk sutures in the peritoneum and posterior sheath and in the anterior rectus sheath. No subcutaneous suture was employed although one deep through-and-through suture penetrating the skin and extending to the anterior rectus sheath was used to collapse dead space and steady the subcutaneous fat which measured 13 centimeters in depth. After the peritoneum was closed, the wound and the subcutaneous fat were thoroughly washed with the mixture of streptomycin (200 units per cubic centimeter) and sulfamylon 5 per cent. Each suture line was also treated with the mixture, by means of a sponge wet with the mixture along with the suture line in the pelvic floor. The perineal wound was not packed with it because of the scarcity of material.

The colostomy was opened on the second day, the temperature rose to 100 degrees and remained there for 2 days. Patient was started on penicillin, 20,000 units per day, on the 5th day, to protect her from pneumonia. On the 6th day, she began to exhibit signs of congestive failure with electrocardiographic evidence of infarction. Sutures were removed from the abdominal wound on the 8th postoperative day. The skin edges separated slightly for a distance of 2 centimeters where the skin edges were inverted but in spite of all the difficulties, the rest of the 25 centimeter incision had healed *per primam* and there was soft white healing.

The patient had a stormy course with her coronary occlusion and later developed thrombophlebitis of both legs although she had daily adequate doses of penicillin. She finally recovered, however, and was discharged on the 52nd day after operation.

In summary, here is a large wound in a very obese woman with cardiac failure who developed all complications to be expected under the circumstances and yet excellent wound healing was obtained. Pathology report returned poorly differentiated carcinoma which had completely destroyed the wall of the rectum but had not invaded the lymph nodes. Excision appeared to be adequate. There is hope, therefore, that something definite was accomplished.

CASE 2. Male, aged 17 years. A diagnosis of inguinal adenitis of unknown etiology was made. Biopsy tissue was removed from node. Patient admitted to the hospital with story that 6 days before the mass had suddenly appeared in left inguinal region. Two days later, patient went to a doctor who claimed to have reduced it. It continued to be painful and tender; but he had no nausea, and did not vomit. Bowel movements were normal. He denied venereal infection.

Physical examination revealed a tender mass 4 centimeters long, in middle of the left inguinal ligament. It lay subcutaneously and was irreducible. No local heat or signs of suppuration were noted and no primary focus was found in the feet or about the genitalia. There was a slight impulse on coughing. The external ring could be felt below the mass. Temperature was 101.6 degrees; white blood cells 11,600; polymorphonuclears, 77 per cent. The preoperative diagnosis was inguinal adenitis with unknown primary focus.

The mass was explored to make sure it was not incarcerated omentum. A large succulent gland was found and the greater portion of it was removed. The residual portion was bathed in sulfamylon, 5 per cent and streptomycin, 200 units per cubic centimeter.

Pathologic report: "Many suppurative areas." Collections of polymorphonuclear leucocytes were noted in necrotic areas. There were areas of marked hyperemia, but no signs of specific infection. The diagnosis was acute suppurative lymphadenitis of the inguinal nodes. Frei test and Wassermann later proved to be negative even though a small lesion was subsequently found on the underside of the shaft of the penis. Dark field examination from this lesion was negative.

Patient was given both sulfadiazine and penicillin parenterally. He continued to run a septic temperature for 10 days. His fever did not respond to sulfadiazine at first and penicillin was started on the 8th day after operation.

The wound healed *per primam*.

Comment: Here is an interesting lesion. Wounds made to secure biopsy tissue from such nodes are notorious for suppurating and invariably open.

CONCLUSIONS

For local chemotherapy sulfamylon, 5 per cent, seems to be superior to the 6 other antibacterial substances tested. It possesses the widest range of antibacterial activity and is relatively nontoxic. It is active in the presence of pus and blood and is not affected by changes in the acidity of the environment. It possesses rapid bactericidal activity. Sulfamylon in a concentration of less than 3 per cent should not be used. Neutralized sulfamylon should be used.

Streptomycin is next best. It failed to attack the streptococcus in concentrations of 200 units per cubic centimeter, and this antibiotic is destroyed by increasing the acidity of the environment. Like sulfamylon, streptomycin acts rapidly in the presence of blood and is relatively nontoxic.

Penicillin is placed third. It is nontoxic, but penicillin is readily destroyed by changes in *p*H and possesses a very narrow range of bacterial activity. Resistant strains are not infrequently encountered and this antibiotic becomes almost worthless in the presence of a mixed infection. Penicillin does not destroy mixed bacteria, and, conversely, penicillin is destroyed.

The mixture of sulfamylon 5 per cent and streptomycin is nontoxic, relatively stable in the wound, and has almost a complete range of bacterial activity including the anaerobes of gas gangrene.

Thirty contaminated wounds have been successfully sutured, after a mixture of sulfamylon and streptomycin was used as a subcutaneous antiseptic. Soft white healing was obtained.

This mixture was used unsuccessfully, however, in the treatment of open wounds containing slough and sequestra. The mixture did not prevent the regrowth of pyocyaneus over the surface of wounds or burns.

Tyrothricin, parachlorophenol, and zephiran have a toxicity which permits their use only on granulating wounds.

A pattern is set forth for a method of investigating the efficacy of antibacterial substances for local chemotherapy of wounds.

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ANOMALOUS INNERVATION OF THE INTRINSIC MUSCLES OF THE HAND

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IT has long been taught that the median nerve innervates four and one-half muscles in the hand, and the ulnar nerve all the rest. Those which are thus classically considered to be supplied by the median nerve are the opponens pollicis, the abductor pollicis brevis, the first and second lumbricales, and the superficial (lateral) head of the flexor pollicis brevis. The ulnar nerve has been considered as supplying the remainder. Yet, it has been long recognized by those dealing with the diagnosis and repair of peripheral nerve injuries that there are definite, and sometimes bizarre, variations as regards the nerve supply to the intrinsic muscles of the hand. This paper, then, is designed in no way to present something entirely new in the knowledge of this subject. Rather, its purpose is to record a few well verified cases of this type, to emphasize again the occurrence of these anomalous innervations, and to stress the importance of their recognition in the diagnosis, treatment, and postoperative evaluation of peripheral nerve injuries.

The neurological surgeons engaged in the management of the casualties of World War I clearly recognized this problem. However, the only specific instance mentioned in the report of the Medical Department in World War I is the occasional "total supply of . . . the first dorsal interosseus by the median nerve"(4). In their excellent book on peripheral nerve injuries, Pollock and Davis (2) refer to the problem of atypical nerve supply to the muscles of the hand, mentioning the occasional total supply of the flexor pollicis brevis by the ulnar nerve and of the first dorsal interosseus, again, by the median nerve. Other than in these works, however, the problem has received scant attention in the literature. In fact, anatomical texts usually fail to mention these occasional anomalous innervations. The only anatomical work which was found to describe branches between the ulnar and median nerves is Poirier and Charpy's *Traite d'Anatomie Humaine.* In this treatise, these anastomoses were described as being single, double, or triple strands, crossing from one to the other between the superficial and deep layers of the flexor muscles of the forearm.

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STATEMENT OF THE PROBLEM

An accurate discussion of the matter of anomalous innervation is completely interdigitated with several other considerations, and cannot be entertained without some reflection upon them. The accurate testing of the individual intrinsic muscles of the hand is, obviously, of paramount importance and will be discussed in some detail. This is the true cornerstone to correct and precise thinking throughout the problem of peripheral nerve injuries. A recognition of what is and what is not clinically feasible in the way of examination of muscles is also of value. Once one has determined by clinical examination exactly which muscles are functioning, he must then turn to a consideration of whether its nerve supply is the usual one or an anomalous one.

ACCURATE TESTING OF THE MUSCLES OF THE HAND

It is an old concept, but an extremely important one, that motion of a part *per se* is of little value in the evaluation of function in a muscle, be it in the hand or elsewhere. One must be able to palpate the tendon or the belly of the muscle in question, must be able to isolate tactually this tendon or belly from neighboring structures, and must be able to feel a tightening of the tendon or contraction in the belly before he can say with any degree

of certainty that a muscle is or is not functioning. If one adheres rigidly to this, it is obvious that one must immediately accept the fact that there are certain muscles in the hand which cannot accurately be tested. It is not the tenet of this paper that such muscles are unimportant or that they do not participate in a return of function following nerve surgery; it is to be stressed, however, that one cannot state accurately whether such muscles, incapable of being tested by the above criteria, are or are not functioning.

As an example, it is often stated that extension of the proximal and distal interphalangeal joints of the fingers is a function of the lumbricalis-interosseus complex to the finger in question. Thus one is tempted to test the function of this complex by eliciting this motion. This is not an accurate test of the complex, because one cannot palpate accurately the tendon or belly involved. If one examines by motion alone, one will be misled by the occasional patient who can extend these interphalangeal joints well with the extensor digitorum communis to the involved finger (Fig. 1). The accompanying photograph shows a patient extending very well the interphalangeal joints of all fingers. At operation, a complete lesion of the ulnar nerve was found as well as mild scarring of the median nerve, both in the upper arm. Stimulation of the median nerve gave a response only in the pronator teres, flexor carpi radialis, flexor digitorum sublimis, flexor digitorum profundus, and flexor pollicis longus. There was no response in any of the intrinsic muscles of the hand. Stimulation of the ulnar nerve, of course, gave no response. Thus it seems reasonable to believe that the extension of the proximal and distal interphalangeal joints in this individual is due to the extensor digitorum communis, a muscle innervated by the radial nerve. Yet if one accepted motion as a criterion of function, one would say that the lumbricalis-interosseus complex was functioning in each finger in this man.

MUSCLES AMENABLE TO ACCURATE TESTING

It is clearly recognized that there is room for disagreement among competent observers as to what muscles can accurately be tested. For purposes of practicability, a certain amount of dogmatism has been adopted in this matter. It is our feeling that it is wise to test only those muscles which one can accurately and critically evaluate; and to admit frankly that one cannot determine with certainty whether or not certain other muscles are functioning.

The *abductor minimi digiti* can be tested accurately in most instances, as both its belly and its tendon of insertion are readily palpable and can be tactually differentiated from surrounding structures. The tendons of the flexor digitorum sublimis and profundus to the little finger occasionally are a bit confusing, but with care one can eliminate this source of error. This muscle is in contrast to the other muscles of the hypothenar eminence, which cannot be singly tested because one cannot tactually differentiate the contracting belly or tendon of one of these muscles from those of its neighboring muscles. Thus, it is impossible to test the *opponens minimi digiti* as a discrete, individual muscle, and to say definitely whether it is or is not functioning.

The *first dorsal interosseus* muscle can probably be tested accurately, for again its muscle belly and tendon can be palpated accurately, and tactually identified and separated from surrounding structures. There is little possibility that the lumbricalis of the index finger might be confused with this interosseus muscle. The *other dorsal interosseus* muscles are difficult to test. Occasionally one may be able to palpate the belly of one of these, particularly the second, but it is usually quite difficult to separate accurately a contraction in such a belly from a contraction in the corresponding tendon of the extensor digitorum communis or of the proper extensor of the finger involved. It is nearly certain that the so called typical interosseus motion, the sideward movement of the digit at the metacarpophalangeal joint, can be reproduced by means of substitution in some individuals with absolutely no interosseus function. Therefore, it has been our belief that the dorsal interosseus muscles, other than the first, cannot accurately be tested. Occasionally it may be possible to do so, but we believe that one will be wrong more often than right

if he attempts to do so. The *volar interossei* are completely incapable of being accurately examined.

In the muscles of the thumb, too, there is some difficulty in accurate testing. It has been said that the *adductor pollicis* can be tested by determining whether or not the individual can perform certain movements of the thumb. As previously stated, however, motion is completely unsatisfactory as a criterion of function in a given muscle. The belly of this muscle can be palpated, often with ease, but it is difficult to tactually separate it from the mass of surrounding contracting structures—including the first dorsal interosseus, the flexor pollicis brevis, and the first lumbricalis. Therefore, to be absolutely accurate, one should probably conclude that this muscle is not amenable to precise testing, although one can usually detect its complete absence. Early return of function in it, however, would seem to be difficult to determine. On the other hand, the *opponens pollicis* muscle can be quite accurately tested in most individuals. Yet, it cannot be tested, under any circumstances, by merely observing the motion of rotation or opposition of the thumb. Many individuals have such a well developed flexor pollicis brevis that they can perform these motions virtually as well as a person in whom all of the thenar intrinsic muscles are functioning. Only by palpating the contracting muscle mass of the opponens pollicis over the radial aspect of the volar surface of the first metacarpal bone can one approach an accurate testing of this muscle. This is because in this region there is usually no muscle mass with which the opponens pollicis can be confused. However, the abductor pollicis brevis muscle overlays the opponens pollicis in its entirety except for this variable, small area of the latter over the radial side of the first metacarpal. Actually then in instances in which this area is very small the opponens cannot definitely be separated from the abductor pollicis brevis, clinically. This poses no serious problem, however, for in so far as we know, the opponens pollicis and the abductor pollicis brevis are innervated by the same nerve—usually the median, of course. What one is actually testing, then, in some instances is the opponens-abductor complex, and, to be strictly accurate, it might be so termed. Because of the relations mentioned, it is probable that the *abductor pollicis brevis* cannot be tested separately from the opponens pollicis. The *flexor pollicis brevis* is tested only with difficulty. Its muscle belly is easily palpated, but there is difficulty in tactually differentiating it from the opponens-abductor complex. When this complex is not functioning, one can usually determine by palpation that the flexor pollicis brevis is contracting; when the complex is also contracting, however, it is virtually impossible to distinguish tactually the short flexor from this opponens-abductor mass.

Fig. 1. Patient with complete ulnar nerve paralysis and complete loss of function in intrinsic muscles of the hand innervated by the median nerve. Note excellent extension of interphalangeal joints.

The *lumbricales* cannot be tested individually for they cannot be palpated. There are characteristic movements produced by their contraction, of course, but the interossei produce these in many instances. In addition, the lumbricales can frequently take over function usually subserved by the interosseus muscles.

If one accurately tests muscles in this fashion, he will not often be confused by substitution, "trick" movements, and the like. He need not then commit to memory any tests of movement which are said to be indicative of function in a given muscle. He need merely palpate with certainty the belly or tendon of the muscle in question, in search of a contraction. If one adheres to this plan, a very conservative one it is true, he will obtain a considerably more accurate idea of the returns of function following peripheral nerve injuries than is otherwise possible.

THE "NORMAL" INNERVATION

Once one has accurately determined that there is function in a muscle, he may then

inquire as to the nerve which is responsible for that function. The classical teaching as to the innervation of the muscles of the hand has been mentioned. From a clinical standpoint, certain changes in this should be made. In view of the difficulty in testing accurately the whole of the flexor pollicis brevis separately from the other thenar muscles, it seems obvious that it is beyond the realm of clinical practicability to separate the superficial (lateral) and deep (medial) heads of this muscle. In our experience, clinically it has been satisfactory to regard this muscle as totally innervated by the ulnar nerve. This is not then considered an anomalous innervation, but rather the normal innervation. The opponens pollicis and the abductor pollicis brevis of course follow the usually taught rules. Electrical stimulation at the operating table shows that the first lumbricalis is normally median in innervation, but the second lumbricalis, just as its corresponding portion of the flexor digitorum profundus (namely, that to the long or middle finger), is nearly always supplied by the ulnar as well as the median nerve. The third lumbricalis, again as its corresponding portion of the flexor digitorum profundus (that to the ring finger), is nearly always supplied by the median as well as the ulnar nerve. As a matter of fact, the flexor digitorum profundus and the lumbricalis to the fifth finger are many times functioning in cases of complete ulnar nerve paralysis, indicating that they too receive considerable overlapping supply from the median nerve in these instances. This again is so frequent as not to be considered an anomalous innervation. Clinically, the hypothenar muscles and the interossei seem in the usual patient to correspond to the classical teaching.

ANOMALIES IN INNERVATION

One anomalous innervation which we have observed is that of the first dorsal interosseus muscle by the median nerve. Earlier, reference was made to two instances of mention of this in the literature. We have personally observed 4 cases of this, in a series of 698 ulnar nerve injuries. It is to be emphasized that we did not personally test each of these 698 cases. It is very probable that many other such instances of this anomaly of innervation occurred in this series of lesions of the ulnar nerve but were not recognized. In each of the 4 patients comprising this group, 1 or more preoperative examinations found the first dorsal interosseus to be contracting; in each at operation the ulnar nerve was found completely severed at some point proximal to the olecranon groove, and in each, one or more postoperative examinations found the first dorsal interosseus still to be functioning. In 3 of these cases, examination of the first dorsal interosseus muscle was done by the method of electrodiagnosis (3) using the Golseth-Fizzell stimulator. In each instance, the muscle showed a response typical of a completely normal muscle which has not had a disturbance in its nerve supply, a further bit of evidence that its innervation was not through the ulnar nerve. Thus, in these cases, the first dorsal interosseus was apparently supplied by a nerve other than the ulnar nerve. In 2 of the cases, it was definitely proved at surgery by stimulation of the median nerve that it was this nerve which supplied the muscle in these particular patients. It seems reasonable to assume that such also was the situation in the other 2 patients.

The route of this anomalous innervation theoretically could be either by way of a branch given from the median nerve to the ulnar nerve in the forearm, or by way of a branch directly to the first dorsal interosseus muscle from the median nerve in the hand. In Case 1, the first situation was found to exist. At operation, the ulnar nerve was found completely divided just proximal to the elbow. Stimulation of the nerve just proximal and just distal to the point of severance gave no response. Stimulation of the median nerve in the upper arm produced the usual median response plus a good contraction in the first dorsal interosseus; in the flexor digitorum profundus muscles to the fourth and fifth fingers, with their corresponding lumbricales; and in what was thought to be the flexor pollicis brevis. The ulnar nerve was then followed down to a level about 6 centimeters distal to the medial epicondyle, to that point where the branches emerge from the ulnar

nerve going to the flexor digitorum profundus. At this location several branches were seen going into the ulnar nerve, coming from beneath the flexor-pronator group of muscles. Stimulation of these branches separately, and stimulation of the ulnar nerve distal to this point—but *not* proximal to it—produced a good contraction in the first dorsal interosseus; in the profundus tendons to the fourth and fifth fingers and also in what was interpreted to be the corresponding lumbricales; and in the flexor pollicis brevis. The neuroma and glioma of the ulnar nerve, together with the fibrous bridge joining them, were resected. Microscopic examination of the tissue was made by Major G. D. Ayer, Jr., using both hematoxylin and eosin, and Bodian stains. The fibrous bridge between the neuroma and glioma was found to be cicatrix, containing no identifiable nerve tissue. Cross-section of the distal end of the glioma showed the usual cross-sectional anatomy of funiculi; however, several bundles of funiculi contained definite axis cylinders. Since none came across the fibrous bridge, these probably represented a few axons growing in a retrograde fashion from the point where the anomalous branches entered the ulnar nerve.

In another patient (Case 2) stimulation of the ulnar nerve above the elbow at operation gave no response; but stimulation of the median nerve in the upper arm gave the usual median response, and in addition a definite strong contraction in the first dorsal interosseus. In this case the actual anomalous branches were not seen, and we do not know with absolute certainty which of the two possible routes of anomalous innervation exists in this individual. However, about 1 month after surgery, the median nerve was blocked at the wrist with novocain. A satisfactory anesthesia in the median distribution was produced and the opponens-abductor complex did not then function. However, the first dorsal interosseus and the flexor pollicis brevis still had good function. Although it is not possible to say with certainty that we totally blocked the nerve in this man, it seems reasonable to assume that such was the case. With such an assumption, one can then conclude that again in this patient, the route of the innervation was through the median nerve in the upper arm and then into the ulnar nerve high in the forearm by way of anomalous branches. Thus, at the wrist the fibers going to these anomalously innervated muscles were contained in the ulnar nerve and not in the median nerve. In 2 other patients (Cases 3 and 4), the median nerve was not stimulated at operation, although in each the ulnar was found completely severed just above the elbow. Each had preoperatively and postoperatively good function in the first dorsal interosseus muscle, and yet stimulation of the severed ulnar nerve at operation in each instance produced no contraction. As stated earlier, it is the assumption in these two cases that the anomalous innervation is also from the median nerve.

A second muscle probably anomalously innervated in two of these cases is the flexor pollicis brevis. It is to be noted that in the patient referred to as Case 1, stimulation of the anomalous branches at operation gave a response in the flexor pollicis brevis as well as in the first dorsal interosseus. In the instance of Case 2, after blocking of the median nerve at the wrist the flexor pollicis brevis continued to contract despite the severance of the ulnar nerve just above the elbow. This contraction would indicate that in these patients fibers to the flexor pollicis brevis came down the upper arm in the median nerve, crossed over in the upper portion of the forearm to join the ulnar nerve by anomalous branches such as noted in Case 1, and then coursed down the forearm in the ulnar nerve. In Case 2, the operator did not note a contraction in the flexor pollicis brevis when the median nerve was stimulated in the upper arm; however, the opponens-abductor complex of course contracted, and this could well have masked the contraction in the flexor pollicis brevis. Therefore, in these 2 cases, the flexor pollicis brevis is very probably anomalously innervated by fibers passing down the median nerve to join the ulnar nerve in the upper one-third of the forearm, just as is the first dorsal interosseus.

A third muscle anomalously innervated in one of these cases is the abductor minimi digiti. In the instance of Case 3, careful preoperative examination and repeated post-

Fig. 2. Case 2. Patient with complete severance of ulnar nerve. Note belly of first dorsal interosseus muscle, being palpated by examiner's left index finger.

Fig. 3. Patient with usual complete ulnar paralysis. Compare area of first dorsal interosseus muscle with that in Figure 2.

operative examinations have shown a normal contraction in the abductor minimi digiti, this despite the complete severance of the ulnar nerve. It is assumed that the muscle is innervated, in this individual, by the median nerve in a manner entirely similar to that here outlined. We did not find this anomalous innervation of the abductor minimi digiti in our other cases.

At this point, it is of significance to note that the ulnar nerve was severed proximal to the forearm in each of these 4 cases. In 2, the evidence is reasonably definite that the route of the anomalous innervation was by way of a branch given from the median nerve to the ulnar nerve in the forearm; it is probably significant that in the remaining 2 cases the lesion was again proximal to the forearm. It is important, then, to realize that, in these instances, if the ulnar nerve were severed at the wrist or in the lower part of the forearm, the fibers traversing this anomalous route would also be severed, and one would find no evidence of such an anomalous innervation.

A fourth anomalous innervation which we have noted is that of the opponens pollicis by the ulnar nerve. We have noted only one definite instance of this in 551 median nerve injuries, but again unrecognized ones very probably were in this group. In this instance (Case 5), the soldier was wounded on August

Fig. 4. Case 3. Patient with complete severance of ulnar nerve in right arm. Note fullness in area of abductor minimi digiti (indicated by pointer) and excellent abduction of fifth finger. Note also lack of first dorsal interosseus muscle atrophy, and lack of any obvious wasting in hand.

Fig. 5. Case 5. Patient with complete severance of median nerve. Note belly of opponens pollicis being palpated by examiner.

26, 1944 in the volar aspect of the right wrist. In early November, 1944, an overseas note stated that there was weak function in the opponens pollicis, but complete anesthesia in the autonomous zone of supply of the median nerve. On November 24, 1944 a suture of the median nerve was done just proximal to the wrist. We observed this man from January 11, 1945 until about October 1, 1945. During this entire time, he had good function in the opponens pollicis. By September 1, 1945, he had also a return of deep sensation in the autonomous zone of the median nerve, and crude, tingling superficial sensation, with no two-point discrimination or stereognosis. At re-exploration on September 17, 1945, electrical stimulation of the median nerve above and below the site of suture gave no motor response; stimulation of the ulnar nerve at the wrist gave the usual ulnar response plus a definite, clear-cut contraction in the opponens pollicis muscle. In this case, therefore, this muscle was supplied by the ulnar nerve. Electrodiagnostic data on the opponens pollicis in this man were those of a completely normal muscle whose nerve supply had not been damaged. Whether in this case the supply to the opponens went into the ulnar nerve from the median nerve somewhere above the wrist, or whether it came all the way down from the brachial plexus in the ulnar nerve, unfortunately we cannot say.

We have observed with certainty then the anomalous innervation of 4 intrinsic muscles of the hand—namely, the first dorsal interosseus, the flexor pollicis brevis, the abductor minimi digiti, and the opponens pollicis. However, it is our opinion that other anomalies in innervation of the intrinsic muscles do occur, and that had we been, in the early part of our experience, more aware of their occurrence we would have found still more such instances in our series of median and ulnar nerve injuries.

APPLICATION TO THE STUDY OF PERIPHERAL NERVE INJURIES

One is able to examine a peripheral nerve injury and to assess its recovery following treatment by determining the presence of motor, vasomotor, and sensory function ascribable to the nerve in question. It is not within the province of this discussion to consider vasomotor and sensory examination. As regards motor examination, it has been stated earlier in this paper that the keystone to this is an accurate testing of the individual muscles supplied by the nerve involved. Yet, it is not sufficient merely to ascertain the presence of function in such a muscle in order to say that a nerve is only partially damaged, or that there has been return of function in such a nerve following suture. One must go further and determine with certainty that the muscle which is contracting is doing so because of impulses traveling down the nerve in question, and not by virtue of an anomalous innervation. That is to say, if after suture of the median nerve at the wrist the opponens pollicis is found to be functioning, it is by no means clear evidence that this is due to return of function in the sutured median nerve. Only by stimulation of the median nerve at the operating table could one say with absolute certainty that the contraction in the opponens pollicis was being mediated through this nerve. Novocain block of the ulnar nerve at the wrist, with preservation of function in the opponens pollicis, and then similar block of the median nerve at this same level with loss of this function, would, however, also give acceptable data. Only when one has done one of these two things, can he say with any degree of assurance that function in an intrinsic muscle of the hand is due to a return of function following neurorrhaphy; or, in preoperative evaluations, to incompleteness of the lesion in the involved nerve. If all cases were examined in this critical manner, one might find less divergence of opinion in regard to the return of function of the intrinsic muscles of the hand following nerve suture.

REPORT OF CASES

CASE 1. A 28 year old private, first class, was wounded in action on June 6, 1944 by enemy shell fragments, sustaining multiple wounds including a penetrating wound of the right elbow, with a compound, comminuted fracture of the distal end of the humerus and damage to the ulnar nerve. There was no vascular damage. In January, 1945, examination showed good function in the first dorsal interosseus muscle, but no function in other muscles usually innervated by the ulnar nerve; there was

complete anesthesia in the autonomous zone of the ulnar nerve. On January 27, 1945, he had the first stage of a full thickness abdominal pedicled flap to the elbow, which was completed March 19, 1945. It was decided that the ulnar nerve was probably not severed due to the motor function above noted, and that exploration of the nerve could be deferred for the moment. Thus, on May 26, 1945, excision of the distal end of the humerus was done, with replacement of this by an acrylic implant; at this procedure the ulnar nerve was found, unexpectedly, to be completely severed 8 centimeters proximal to the medial epicondyle. Because the positioning of the arm necessary after this orthopedic procedure would not permit neurorrhaphy, the orthopedist performed a bulb suture of the nerve at this time. The postoperative course was uneventful. Examination on August 13, 1945 again showed good function in the first dorsal interosseus, but not in other muscles usually innervated by the ulnar nerve; there was total anesthesia in the autonomous zone of the nerve. On September 6, 1945 the ulnar nerve was re-explored. Several small branches were found entering the ulnar nerve about 8 centimeters distal to the medial epicondyle, at that point where the branches to the flexor digitorum profundus usually come off the nerve; these branches came beneath the superficial flexor-pronator group and presumably came from the median nerve. Stimulation of these branches themselves, and of the ulnar nerve distal to the point of their entrance into the nerve, gave good contraction in the flexor digitorum profundus to the fourth and fifth fingers and the lumbricales to these fingers; in the first dorsal interosseus; and in the flexor pollicis brevis. Stimulation of the median nerve in the upper arm gave the usual median response plus the above. Stimulation of the ulnar nerve at any point proximal to the entrance of these branches failed to give any muscular contraction. Electrodiagnostic analysis by the use of Golseth-Fizzell stimulator showed in the first dorsal interosseus muscle a response which was typical of a normal muscle with an intact and uninjured nerve supply.

CASE 2. An 18 year old private was wounded in action on March 5, 1945 by enemy mortar shell fragments, suffering a penetrating wound on the medial aspect of the left upper arm, with no fracture and no significant vascular damage. A muscle and sensory examination on April 17, 1945 is recorded as showing no function in the ulnar nerve, with the exception of a contraction in the first dorsal interosseus muscle. All other nerves in the arm were intact. On July 9, 1945 at operation there was found to be a complete severance of the ulnar nerve 10 centimeters proximal to the medial epicondyle, with a gap of 4.8 centimeters between the proximal neuroma and distal glioma; a neurorrhaphy was done. On August 22, 6 weeks after suture, it was found that there was definite function in the first dorsal interosseus muscle (Figs. 2 and 3). Re-exploration was done on August 30, 1945 at which time stimulation of the ulnar nerve just proximal to, and just distal to, the point of suture produced no muscular contraction; the nerve was not stimulated in the forearm. Stimulation of the median nerve in the upper arm gave the usual median response plus contraction in the first dorsal interosseus muscle. On November 5, 1945, the median nerve was blocked at the wrist with novocain, producing sensory anesthesia in the median distribution; loss of function in the opponens-abductor complex; and preservation of function in the first dorsal interosseus and in the flexor pollicis brevis muscles. An attempt was made to block the ulnar nerve at the wrist, but this was unsuccessful. Electrodiagnostic analysis by means of the Golseth-Fizzell stimulator showed in the first dorsal interosseus muscle a response which was typical of a normal muscle with an intact and uninjured nerve supply; and in the abductor minimi digiti a response which was typical of a muscle whose nerve supply had been damaged.

CASE 3. A 34 year old private, first class, was wounded in action on January 13, 1945 by enemy shell fragments, suffering a penetrating wound of the posteromedial aspect of the right elbow region, with no fracture and no significant vascular damage. Routine examinations on May 10, 1945 and August 28, 1945 are recorded as showing contraction in the first dorsal interosseus muscle. On September 13, 1945 at operation, the ulnar nerve was found completely divided just proximal to the olecranon groove, and a neurorrhaphy was performed. Examination on October 15, 1945 again showed a strong contraction in the first dorsal interosseus muscle, probably in the second as well, and definitely in the abductor minimi digiti. There was amazingly little atrophy anywhere in the hand (Fig. 4). There was complete anesthesia in the autonomous zone of the ulnar nerve. Electrodiagnostic analysis by the Golseth-Fizzell stimulator in this case showed in the first dorsal interosseus muscle, and in the abductor minimi digiti a response which was typical of a normal muscle with an intact and uninjured nerve supply.

CASE 4. A 23 year old sergeant was wounded in action on November 30, 1944 by an enemy machine gun bullet, sustaining a penetrating wound of the middle one-third of the upper arm with no fracture and no vascular damage. Examination in March of 1945 is recorded as showing good contraction in the first dorsal interosseus muscle, with no function in the other muscles usually innervated by the ulnar nerve and with complete anesthesia in the autonomous zone of the ulnar nerve. At operation on April 11, 1945, the ulnar nerve was found to be completely severed 12 centimeters proximal to the medial epicondyle; stimulation above and below the level of injury gave no response. A neurorrhaphy was done without transplantation of the nerve. Postoperatively he continued to have a good contraction in the first dorsal interosseus muscle. This man wished not to have novocain block of the nerves, so this procedure was not carried out. A

satisfactory electrodiagnostic analysis was not obtained in this case.

CASE 5. A 26 year old private, first class, was wounded in action August 26, 1944 by an enemy rifle bullet, sustaining a penetrating wound of the volar aspect of the right wrist with a compound, comminuted fracture of the distal end of the ulna but no significant vascular damage. Examination in October, 1944, is recorded as showing a weak contraction in the opponens pollicis and complete anesthesia in the autonomous zone of the median nerve. The ulnar nerve was clinically intact. On November 24, 1944 a neurorrhaphy of the median nerve was done at the wrist. In January, 1945, examination showed good function in the opponens pollicis muscle, and repeated examinations since that time have confirmed this (Fig. 5). On September 17, 1945, the median and ulnar nerves were re-explored at the wrist. Stimulation of the median nerve just proximal to and just distal to the site of anastomosis gave no motor response; stimulation of the ulnar nerve gave the usual ulnar response plus a strong, definite contraction in the opponens pollicis muscle. Electrodiagnostic analysis showed in the opponens pollicis a response typical of normal muscle with an uninjured and unimpaired nerve supply.

SUMMARY

The occurrence of anomalous innervation of the first dorsal interosseus muscle, of the flexor pollicis brevis, and of the abductor minimi digiti by the median nerve, and of the opponens pollicis by the ulnar nerve, is definitely proved. The recognition of such anomalies, combined with precise testing of the intrinsic muscles of the hand, will make for a more accurate assessment of peripheral nerve injuries, and of the return of function in such injuries after surgical intervention.

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RECONSTRUCTIVE OPERATIONS FOR BENIGN STRICTURE OF THE BILE DUCTS

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THE problem of benign stricture of the bile ducts may be summarized today as it was by Judd, McIndoe and Marshall, in 1931, when they stated, "Traumatic stricture of a bile duct is a tragic accident which entails untold misery for the patient, presents a formidable task to the surgeon and even with the best treatment attempts at reconstruction are followed by high mortality."

The incidence of operations for benign stricture of the bile ducts is low when compared with the large number of biliary operations that are performed. Nevertheless, the physician is deeply concerned with this problem because in the majority of cases a previous crippling biliary operation has been performed on a patient near the middle of life, which will leave that patient in a lethal situation unless it can be corrected by further surgical treatment. Most important of all, the best treatment of benign stricture is prevention.

This study is concerned with a total of 188 cases of benign stricture of the bile ducts in which 218 reconstructive operations were performed at the Mayo Clinic during a 10 year period from 1933 through 1942. Data on 39 patients reviewed in this study have been previously reported by Walters and Lewis. The purpose of this study is to attempt to evaluate a series of reconstructive operations that have been performed under similar circumstances by a group of ten surgeons.

HISTORY

Langenbuch conducted many investigations of the gall bladder and became convinced that cholecystectomy is a feasible operation. He reported the first successful cholecystectomy in 1882. Von Winiwarter in the same year reported the first short-circuiting operation for obstruction of the bile ducts by performing cholecystojejunostomy in six stages. Judd and McIndoe credited Courvoisier with performing the first choledochostomy in 1884. In 1890, Kocher anticipated performing choledochoduodenostomy in a case in which he performed cholelithotrity but he never completed the procedure. In 1891, Sprengel reported the first successful choledochoduodenostomy at the Twentieth German Surgical Congress in Berlin. The patient was well and working 6 months after the operation. In 1905, W. J. Mayo (13) reported the first successful hepaticoduodenostomy. His patient was reported alive and well 18 years later (15). Many others in addition to the foregoing contributed much to the early development of surgical treatment of the biliary system. This brief historical sketch reveals that the foundation for the surgical management of biliary disease and its complications was established in the brief span of 23 years.

Benign stricture was early recognized to be a cause of biliary obstruction, for Sprengel mentioned this possibility in his paper. As time passed and biliary surgical treatment increased, we may detect the increase of cases of benign stricture from the attention given the problem in the literature. Many excellent contributions and reviews have been presented, notably by Jacobson, Eliot (2,3), Mayo (14,15), Judd and his associates (6,7,10), Walters (17), Walters and Lewis (18) and Horgan. An exhaustive review of the literature is not in the scope of this study, as this has been amply covered by other writers.

INCIDENCE

The fact that benign stricture of the bile ducts is predominantly a disease of midlife adds importance to a consideration of this condition. The age of the patients (Table I) in this study varied from 20 to 73 years and

From the Division of Surgery, Mayo Foundation and Division of Surgery, Mayo Clinic.

TABLE I.—AGE DISTRIBUTION OF PATIENTS WHO HAD BENIGN STRICTURE OF THE BILE DUCTS

Age, yrs.	Patients	
	Number	Per cent
20 to 29	18	10
30 to 39	47	25
40 to 49	65	35
50 to 59	33	17
60 to 73	25	13

the average age was 44.5 years. Sixty per cent of all patients were 30 to 49 years old, while 30 per cent were in the age group of 50 years and older.

The patients were predominantly women, as is characteristic of cholecystic disease. One hundred and forty-five patients (77 per cent) were women and 43 patients (23 per cent) were men. The ratio of women to men was 3.4:1.

TABLE II.—FREQUENCY DISTRIBUTION OF PATIENTS BY NUMBER OF BILIARY OPERATIONS PERFORMED PRIOR TO ADMISSION DURING PERIOD OF STUDY

Operations	Number	Patients	
		Number	Per cent
0	0	2	1
1	105	105	56
2	140	70	37
3	33	11	6
Total	278	188	100

It is well known that benign strictures are practically always associated with a history of previous biliary surgical treatment. However, the multiplicity of surgical procedures which patients who have benign strictures have undergone has not been so widely recognized. All but 2 patients in the study had undergone previous biliary operations. The

TABLE III.— ANALYSIS OF PREVIOUS BILIARY OPERATIONS

Procedures	Patients	Previous operations performed at clinic
Cholecystectomy (simultaneous choledochostomy, 31)	102	6 cholecystectomy
Cholecystectomy; choledochostomy	27	2 cholecystectomy
		2 choledochostomy
Cholecystectomy; choledochostomy (twice)	4	1 choledochostomy*
		2 choledochostomy†
Cholecystectomy; choledochostomy; laparotomy	1	1 laparotomy
Cholecystectomy; choledochostomy; reconstruction over catheter	1	
Cholecystectomy; choledochostomy; choledochoduodenostomy	3	
Cholecystectomy; choledochoduodenostomy	0	1 choledochoduodenostomy
Cholecystectomy; reconstruction of common duct	5	
Cholecystectomy; laparotomy	17	3 laparotomy
Cholecystectomy; hepaticostomy	3	
Cholecystectomy; transplanting external fistula; laparotomy	1	
Cholecystostomy; cholecystectomy	11	1 cholecystectomy
Cholecystostomy	1	
Cholecystostomy; choledochostomy	1	
Choledochostomy	1	
Choledocholithotomy	1	
Removal of adenoma of head of pancreas; cholecystostomy; choledochoduodenostomy	1	1 cholecystostomy
		1 choledochoduodenostomy
No operation	2	
Total	188	21

*First choledochostomy was performed at clinic.
†Second choledochostomy was performed at clinic.

TABLE IV.—FACTORS PERTINENT TO ETIOLOGY

Factors	Patients	Per cent
Immediate postcholecystectomy symptoms not classified below	110	58
Extensive strictures (chronic obliterative cholangitis); symptoms began 1 to 10 months after cholecystectomy	22	12
History of definite surgical trauma	17	9
Short isolated strictures of the common duct	11	6
Indeterminate	10	5
Onset of symptoms 3 to 12 years after cholecystectomy	6	
Strictures attributable to gall stones	3	
Common duct stone associated with stricture 12 years after cholecystectomy	1	10
Spasm of sphincter of Oddi	5	
Chronic pancreatitis	2	
Surgical removal of adenoma of the head of the pancreas	1	
Total	188	100

entire group of 188 patients had undergone 278 biliary operations (Tables II and III) prior to the reconstructive procedure with which this study is concerned. Two hundred and fifty-seven of these operations were performed elsewhere. Eighty-one patients had undergone two or three biliary operations prior to admission. In 181 cases (96 per cent) cholecystectomy had been performed 2 weeks to 14 years or an average of 24 months prior to the final reconstructive operation. In 107 cases (59 per cent of 181 cases) 1 year or less had elapsed between cholecystectomy and the final reconstructive operation. In 9 cases cholecystectomy had been performed at the clinic. Seventeen patients had undergone unsuccessful reconstructive operations prior to admission to the clinic for the final operation; 2 of these operations had been performed at the clinic prior to 1933.

ETIOLOGY

It was recognized early in the history of cholecystectomy that traumatic stricture of the bile ducts is a complication with which one must be concerned. However, Judd (6) and Judd and Olson (9) maintained that one could not attribute all strictures of the bile ducts occurring after cholecystectomy to trauma at the time of cholecystectomy. Their thesis was based on the fact that frequently at either primary or secondary operation one observes an extreme narrowing or a total obliteration of the extrahepatic ducts and in certain cases the obliterative process extends into the intrahepatic duct system. In these cases the patients, even though exhibiting extensive obliterative changes, often give a history of being free of symptoms 3 to 9 months after cholecystectomy. This lesion is difficult to explain on a basis of trauma and Judd attributed it to obliterative cholangitis.

In 22 cases (12 per cent) obstructive symptoms developed (Table IV), ranging from 1 to 10 months after cholecystectomy and averaging 5 months. The patients had enjoyed an uneventful convalescence prior to the onset of symptoms. At surgical exploration they displayed an extensive obliteration of the extrahepatic ducts. Chronic obliterative cholangitis is the most likely explanation in this group of cases. A number of additional patients who had persistent postoperative fistula and others following multiple operations demonstrated extensive obliterative changes in the ducts, but we are unable to determine what portion, if any, of these changes may be attributed to obliterative cholangitis.

In one case in this study it was observed that trauma may be associated with extensive obliteration. The patient stated when first seen at the clinic that the common duct had been severed at the time of cholecystectomy and that the surgeon had reconstructed the duct over a T tube. The patient was free of symptoms for 6 months, after which obstructive symptoms began. Twelve months later at re-exploration an extensive stricture of the extrahepatic duct system was encountered. It is impossible to be certain whether this condition followed the injury or resulted from chronic inflammation. However, in view of the extent of the stricture one would be led to believe that it could best be explained on a basis of chronic inflammation probably secondary to the injury.

Another etiologic factor which has been considered previously by others is ulceration of the epithelium of the common duct produced by an embedded gall stone. This is oc-

casionally a factor but apparently a minor one, since in only 12 cases in this study was there a history of calculi having been present in the common duct at the primary operation and in only 14 additional cases were calculi found in the common duct at the time of the reconstructive operation. One patient in the latter group had been free from symptoms for 12 years after cholecystectomy and this stricture probably arose from a calculus in the common duct. It is conceivable that a number of strictures in these cases resulted from injury at the previous cholecystectomy. However, in 3 of the cases in which there was no history of previous cholecystectomy we have additional positive evidence that stricture resulted from embedded gall stones. In one case there was a fistula between the common duct and the duodenum after cholecystostomy had not produced relief of symptoms. A choledochoduodenal fistula existed in another case in which a previous biliary operation had not been performed. The gall bladder in this case was atrophic. In the third case, in which operation had not been performed previously, there was a stricture at the site of the junction of the cystic duct with the common duct which was associated with hydrops of the gall bladder.

The most significant factor in the production of benign stricture is trauma to the bile ducts at the time of cholecystectomy. This is evident when we recall that in 181 cases (56 per cent) cholecystectomy had been performed and that in 5 other cases some other biliary operation had been performed, leaving only 2 patients without a history of biliary operation. The evidence is convincing when we learn that in 110 cases obstructive symptoms developed immediately after cholecystectomy and that in an additional 17 cases (9 per cent) the patient gave a definite history that the bile ducts had sustained surgical trauma at the time of cholecystectomy. In 11 additional cases in which surgical trauma is a likely factor there were isolated strictures not associated with stones and so located that choledochocholedochostomy over a T tube was performed. Therefore, in at least 138 cases (73 per cent) the factor of surgical trauma is strongly suggested.

TABLE V.—ANALYSIS OF LESIONS FOUND AT CHOLECYSTECTOMY

Lesion*	Operation at clinic, cases	Total cases	Per cent
Cholelithiasis only	5	119	71
Cholelithiasis and choledocholithiasis	2	9	
Record indicated only absence of stones		20	11
No record of lesion available		22	12
Acute cholecystitis with stones	2	3	
Acute cholecystitis only		3	
Common duct stone		3	
Stricture of common duct		1	
Strawberry gallbladder		1	
Total	9	181	100

*Information not always complete in history.

The remaining cases fall into the following etiologic groups: an indeterminate group of 10 cases; a group of 6 bizarre cases in which the patients were free of symptoms for 3 to 12 years after cholecystectomy and then, after various operations on the common duct had been performed, strictures were found when exploration was done at the clinic; a group of 5 cases in which severe spasm of the sphincter of Oddi was diagnosed by the surgeon; 2 cases in which stricture resulted from chronic pancreatitis. Obstruction of the common duct followed the removal of an adenoma from the head of the pancreas in the case of another patient.

CHOLECYSTOSTOMY AND CHOLEDOCHOSTOMY

Cholecystostomy rather than cholecystectomy has been recommended in certain cases in which there is severe inflammation of the gall bladder and cholecystectomy would be difficult. This recommendation is borne out by the fact that only 14 of the patients (7.4 per cent) gave a history of cholecystostomy, while 11 of these had undergone cholecystectomy subsequently prior to admission to the clinic. Thirty-one patients gave a history of choledochostomy carried out at the time of their cholecystectomy; in approximately a half of these cases immediate postoperative obstructive symptoms developed. Cholecystostomy and choledochostomy appear to be of minor importance in the causation of benign stricture.

TABLE VI.—SYMPTOM PATTERNS AFTER CHOLECYSTECTOMY

Symptom patterns	Patients	Per cent
Immediate postoperative jaundice only	14	8
Immediate postoperative biliary fistula persisting until secondary operation	54	30
Immediate postoperative biliary fistula closing spontaneously followed by obstructive symptoms	51	28
Symptom free 1 to 12 months prior to onset of obstructive biliary symptoms	49	27
Symptom free 3 to 12 years prior to onset of obstructive biliary symptoms	12	6
Spontaneous occurrence of biliary fistula at second postoperative month	1	1
Total	181	100

TABLE VII.—NO PREVIOUS CHOLECYSTECTOMY

Previous operation on biliary tract	Condition present at time of reconstructive operation	Cases
None	Choledochoduodenal fistula with stricture	1
	Hydrops of gall bladder and stricture	1
Cholecystostomy	External biliary fistula due to common duct stone and stricture*	1
	Choledochoduodenal fistula with stricture	1
Choledochostomy	Common duct stones and stricture	1
Choledocholithotomy and drainage of gallbladder	Common duct stone with stricture	1
Removal of adenoma of head of pancreas	Obstruction of common duct due to pancreatitis	1
Total		7

*Choledochostomy had also been performed on this patient.

LESIONS FOUND AT CHOLECYSTECTOMY

Since approximately 73 per cent of benign strictures appear to be the result of a surgical accident, cholecystectomy is not warranted unless clinical findings indicate the presence of a diseased gall bladder. Twenty (11 per cent) of the patients (Table V) in this study who had undergone cholecystectomy had a definite history of absence of gall stones. In 22 cases (12 per cent) the history did not mention either the absence or presence of gall stones. In 128 cases (71 per cent) there was a definite history of the presence of gall stones recorded as the only pathologic condition present. In 11 cases (6 per cent) cholecystectomy was performed for acute cholecystitis, strawberry gall bladder, stricture of the common duct, or stone in the common duct. Thus in all, 77 per cent of the patients had lesions requiring cholecystectomy. In at least 11 per cent and possibly more of the cases, cholecystectomy was not associated with the presence of gall stones. Traumatization of the bile ducts does not occur frequently but, when it does occur, it is a real tragedy. The possibility of this tragic complication should be considered in evaluating the indications for cholecystectomy and should reduce the number of stoneless and nonpathologic gall bladders that are removed.

CHOLECYSTECTOMY PERFORMED AT THE CLINIC

In 9 of the 181 cases cholecystectomy was performed at the clinic. Drainage of the common duct by a T tube was also instituted in 7 cases for 1 to 3 months. Stones were present in 9 gall bladders and in 2 common ducts. There was acute cholecystitis in 2 cases.

At the time of reconstructive operation 5 patients were found to have a benign stricture and one of these patients exhibited a generalized obliteration of the extrahepatic ducts. Three patients were found to have a narrowing of the sphincter of Oddi; the symptoms developed 3 months, 5 years, and 11 years, respectively, after cholecystectomy. In the remaining case the diagnosis was chronic pancreatitis with secondary biliary obstruction at operation 7 years after cholecystectomy.

SYMPTOMS

Symptoms are analyzed separately for the 181 cases in which there was a history of cholecystectomy (Table VI), and for the 7 cases in which the patients had not undergone cholecystectomy previously (Table VII).

The 181 cases in which cholecystectomy had been performed previously present 5 definite symptomatologic groups. In the first group of 14 cases (8 per cent of 181 cases) jaundice developed immediately after cholecystectomy as the only symptom and persisted until exploration was performed. Surgical injury to the common duct in this group is obvious.

In the second group of 54 cases (30 per cent) biliary fistula developed immediately after cholecystectomy and persisted until a second-

ary operation was performed. In this group of cases there were recurrent obstructive symptoms which were associated with temporary malfunction of the fistula.

In 1 case a spontaneous fistula developed during the second postoperative month and persisted until a secondary operation was performed.

In the third group of 51 cases (28 per cent) a biliary fistula developed immediately after cholecystectomy but spontaneously closed within 1 to 14 months. Following closure of the fistula typical obstructive symptoms developed and persisted. In a total of 106 cases a postoperative biliary fistula developed. In 51 of these cases the fistula had closed prior to secondary operation. Many other fistulas probably would have closed if the surgeon had deferred operation.

In the fourth group of 49 cases (27 per cent) convalescence was normal for 1 to 12 months and then obstructive symptoms developed. Actually in 41 of these cases symptoms developed within 3 to 9 months. This group is composed of the 22 which we have classified as being cases of obliterative cholangitis, 11 in which choledochocholedochostomy over a T tube was performed for isolated strictures and a miscellaneous group in which lesions followed a history of surgical trauma or previous multiple operations or were attributed to a spasm of the sphincter of Oddi.

In the fifth group of 12 cases (6 per cent) symptoms did not develop until between 3 and 12 years after cholecystectomy. This proves a bizarre group in which the strictures cannot be related directly to the cholecystectomy. In 3 cases there was severe spasm of the sphincter of Oddi, in 2 there was stricture following choledochostomy for recurrent colic, in 2 the patients stated that strictures had followed choledochostomy and choledochoduodenostomy. In 1 case jaundice developed 6 years after cholecystectomy and a stricture followed choledocholithotomy. In another the patient gave a history of choledochocholedochostomy performed after 7 years of freedom from symptoms following cholecystectomy. In 1 case the patient could be classified as having chronic pancreatitis and in 1 case there was a history of surgical trauma. In another case the patient, after enjoying 12 years of good health following cholecystectomy, was found to have a stone in the common duct associated with stricture.

One can conclude that in approximately all cases of benign stricture related to cholecystectomy symptoms will develop within a few weeks; in those cases in which symptoms develop after this, other factors appear to be involved in the causation of the stricture.

The 7 cases (4 per cent of 188 cases) in which cholecystectomy had not been performed previously (Table VII) present the following findings: In 2 of this group in which a previous biliary operation had never been performed inflammatory strictures were present. The first patient complained of 3 years' history of fever, loss of weight, anemia and pain in the upper part of the abdomen. An adherent atrophic gall bladder and a strictured common duct were observed, with a fistula between the common duct and the duodenum. The second patient had suffered from recurrent attacks of colicky pain associated with jaundice for a period of 2 years and was found to have a stricture at the junction of the cystic and hepatic ducts associated with hydrops of the gall bladder.

In 2 cases there were strictures after cholecystostomy. A biliary fistula persisted in 1 case after cholecystostomy, and subsequent surgical exploration and choledochostomy had failed to provide relief. When exploration was performed at the clinic a stricture was found in the common duct, associated with a stone. In the other case recurrent colics persisted after cholecystostomy. When exploration was performed at the clinic a stricture was found to be present, associated with a fistula between the common duct and the duodenum.

One patient had undergone unsuccessful choledochostomy for jaundice. The surgeon had reported a shrunken fibrotic gall bladder, which was not removed. Subsequent exploration at the clinic revealed a stricture associated with stones in the common duct.

Another patient had undergone choledocholithotomy, at which time the surgeon reported a ruptured gall bladder, which was not removed. A stricture was found asso-

TABLE VIII.—SYMPTOMS AFTER CHOLECYSTECTOMY

Symptoms	Patients	Per cent
Jaundice	158	87
Biliary fistula	106	59
Acholic stools	89	49
Chills and fever	79	44
Pain	69	38
Nausea and vomiting	41	23
Diarrhea	19	10
Hemorrhage	11	6
Pruritus without jaundice	2	2
Ascites	1	
Jaundice or biliary fistula or both	179	99
Pain alone	2	1
Total	181	

ciated with stones in the common duct when exploration was performed at the clinic.

The remaining patient had had an adenoma removed from the head of the pancreas. After this operation neither cholecystostomy nor choledochoduodenostomy gave relief from the biliary obstructive symptoms. At the final operation an obstructed common duct accompanied by pancreatitis was found to be present.

Three of the foregoing patients presented strictures of the biliary ducts probably attributable to stones. Evidence remained of the previous existence of stones. Three additional patients had stones in the common duct associated with strictures; but they also had had previous explorations of the common duct prior to exploration and we cannot be certain as to the cause of these strictures. One remaining case presents an obstruction following the removal of an adenoma from the head of the pancreas.

DISTRIBUTION OF SYMPTOMS

Of the 181 patients (Table VIII) who had undergone previous cholecystectomy, 179 gave a history of a biliary fistula or jaundice or both. The remaining 2 patients complained of recurrent colicky pain. One of these had a constricted sphincter of Oddi and the other an incomplete stricture of the common duct.

The most frequent symptom, a history of jaundice, occurred in 158 cases (87 per cent). Jaundice developed within a few days after cholecystectomy in 64 cases (41 per cent of 158 cases), while in 94 cases (59 per cent) jaundice developed subsequent to the second postoperative week. Two weeks to 6 months elapsed before 76 patients observed jaundice and 18 did not become jaundiced for 6 months to 7 years after the cholecystectomy. The average concentration of bilirubin for 145 patients (80 per cent of 181 patients) who had elevated levels on admission was 9.1 milligrams per 100 cubic centimeters of serum.

A history of the presence of an external biliary fistula was the second most common symptom and occurred in 106 cases (59 per cent of 181 cases). A fistula persisted after cholecystectomy to the time of secondary operation in 55 cases; in 1 case in this group a spontaneous fistula developed 2 months after operation. In 51 cases the biliary fistula closed spontaneously in 1 month to 14 months. The fistula closed in 4 to 6 weeks in 24 cases but failed to close in 27 cases until 6 weeks to 14 months had elapsed. For the frequency of other symptoms the reader is referred to Table VIII.

Fourteen patients who had jaundice alone immediately after operation and 105 patients whose biliary fistula persisted after cholecystectomy constitute a total of 119 patients (66 per cent) that had symptoms immediately after cholecystectomy. More than a third of the patients complained of pain, a fact which makes the differential diagnosis from a stone in the common duct difficult in a number of cases. The occurrence of diarrhea in 10 per cent of the cases is not surprising, when one considers the disturbance of the digestion and absorption of fat that arises because of the absence of bile and the alteration of pancreatic excretion in certain cases, as a result of chronic pancreatitis. The marked disturbance of the general health of the patients is emphasized by the 6 per cent who gave a history of hemorrhages and the 80 per cent who were admitted with elevated serum bilirubin. Among patients that have deep jaundice and in particular those without a history of biliary fistula, one has difficulty in distinguishing be-

TABLE IX.—SUMMARY OF FOLLOW-UP DATA IN 188 CASES OF RECONSTRUCTIVE BILIARY OPERATIONS AT THE CLINIC*

Surgical procedure	Well last report	Per cent	Obstructive symptoms last report	Per cent	Hospital deaths	Per cent	Deaths after dismissal	Per cent	Total deaths	Per cent	Information not available	Per cent	Total
Hepaticoduodenostomy	19	28	28	42	4	6	13	19	17	25	3	5	67
Choledochoduodenostomy over a rubber tube	21	55	8	21	4	11	5	13	9	24	0	0	38
Choledochoduodenostomy without a rubber tube	10	62	2	13	1	6	2	13	3	19	1	6	16
Reconstruction of common duct over T tube	13	40	10	30	4	12	6	18	10	30	0	0	33
Transplantation of external biliary fistula	0	0	3	50	1	17	2	33	3	50	0	0	6
Hepaticostomy	4	21	4	21	6	32	4	21	10	53	1	5	19
Hepaticojejunostomy	1		1		0		2		2		0		4
Choledochogastrostomy	0		1		1		0		1		0		2
Hepaticogastrostomy	0		1		1		0		1		0		2
Cysticoduodenostomy	0		1		0		0		0		0		1
Total	68		59		22		34		56		5		188
Per cent	36		31		12		18		30		3		

*Thirty additional reconstructive procedures were performed during the 10 year period of study at the clinic.

tween a patient who has obstructive cancer of the head of the pancreas or the ampulla of Vater and one who has a benign stricture. However, the onset of deepening jaundice following a biliary operation should usually rule out the factor of malignancy, but not always.

SUMMARY OF FOLLOW-UP

A follow-up was possible in 183 of the 188 cases. We were able to trace 92 per cent for 3 to 12 years while but 8 per cent of those traced were heard from 1 to 2 years after operation.

An analysis of follow-up reports (Table IX) reveals that a total of 56 patients (30 per cent) were dead, 59 (31 per cent) had symptoms of biliary obstruction and 68 (36 per cent) were reported as being free of symptoms. No information was available for 5 patients (3 per cent). Nine patients were reported to be well 10 to 12 years after surgical treatment, while 4 patients were alive after having had attacks of biliary obstruction and cholangitis for as long as 10 to 12 years (Table X).

Thirty (51 per cent) of the patients who had persistent postoperative biliary obstruction underwent further surgical reconstructive efforts at the clinic as follows: hepaticoduodenostomy, 15; choledochoduodenostomy, 4; reconstruction over a T tube, 3; transplantation of external biliary fistula, 2; hepaticostomy, 6. Six of these patients were free of symptoms at the time of the latest report, there being 2 each who had undergone hepaticoduodenostomy, choledochoduodenostomy and reconstruction over a T tube. Follow-up data are not available for 3 patients.

Thirty (44 per cent) of the patients reported as being free of symptoms at the time of the latest report gave a history of having had symptoms of biliary obstruction in the early postreconstruction period while 38 patients (56 per cent) had remained entirely free of symptoms after the reconstructive operation.

Complications occurred (Table XI) in 18 cases (10 per cent). The diseases were as follows: pneumonia, 6; cerebral accident, 2; parotitis, 3; cholangitis, 3; hemorrhage, 1; cardiac decompensation, 1; atelectasis, 1; pleural effusion, 1; empyema, 1; duodenal fistula, 1; peritonitis, 1; pneumothorax, 1. Four patients had two complications each.

Twenty-two patients (12 per cent) died in the hospital following operation. The causes of death were as follows: hepatic insufficiency, 8; hemorrhage, 5; peritonitis, 2; pneumonia, 2; coronary occlusion, 1; uremia, 1; hepatic

TABLE X.—FOLLOW-UP DATA FOR PATIENTS WHO WERE WELL AT LAST REPORT AND THOSE WHO HAD OBSTRUCTIVE SYMPTOMS AT LAST REPORT

Surgical procedure	Well last report										Symptoms last report							
	1-2 yrs.*		3-5 yrs.		6-9 yrs.		10-12 yrs.		Total	Per cent§	No further surgical procedure				Further surgical procedure		Total	Per cent§
	+Symptoms†	−Symptoms‡	+Symptoms	−Symptoms	+Symptoms	−Symptoms	+Symptoms	−Symptoms			1-2 yrs.	3-5 yrs.	6-9 yrs.	10-12 yrs.	1-2 yrs.	3-5 yrs.		
Hepaticoduodenostomy	0	2	2	5	4	5	1	0	19	28	2	5	4	3	11	3	28	42
Choledochoduodenostomy over a rubber tube	0	2	6	2	5	5	0	1	21	55	0	3	0	0	4	1	8	21
Choledochoduodenostomy without a rubber tube	0	1	2	2	1	4	0	0	10	62	0	2	0	0	0	0	2	13
Reconstruction of common duct over T tube	0	0	1	2	1	2	2	5	13	40	0	4	0	1	4	1	10	30
Transplantation of external biliary fistula	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	3	50
Hepaticostomy	0	0	4	0	0	0	0	0	4	21	0	0	1	0	1	2	4	21
Hepaticojejunostomy	0	0	1	0	0	0	0	0	1		1	0	0	0	0	0	1	
Choledochogastrostomy	0	0	0	0	0	0	0	0	0		1	0	0	0	0	0	1	
Hepaticogastrostomy	0	0	0	0	0	0	0	0	0		0	1	0	0	0	0	1	
Cysticoduodenostomy	0	0	0	0	0	0	0	0	0		1	0	0	0	0	0	1	
Total	0	5	16	11	11	16	3	6	68	36	5	15	5	4	23	7	59	31
Per cent	0	7	24	16	16	24	4	9			8	26	8	7	39	12		

*Years from surgical procedure to last report.
†Patient had had symptoms after surgical procedure.
‡Patient had not had symptoms after surgical procedure.
§Percentage of all patients on whom specified surgical procedure had been performed.

abscess, 1; pyemia, 1; subdiaphragmatic abscess, 1.

Thirty-four patients (18 per cent) died from the following causes after dismissal: hepatic insufficiency, 16; unknown, 8; hepatic abscess, 2; adenocarcinoma of the uterus, 1; esophageal malignant lesion, 1; during biliary operation elsewhere, 1; ruptured spleen, 1; cardiac disease, 1; cerebral hemorrhage, 1; pneumonia, 1; hemorrhage, 1. Twenty of the deaths at home were directly attributable to the biliary lesion. Hemorrhage caused 6 of the entire number of deaths. These deaths occurred prior to the clinical use of vitamin K preparations and one would expect this factor to appear less often in the future as a cause of death than it has appeared in the past.

For the results of the various surgical procedures at the time of the latest report the reader is referred to Tables IX and X. The best results appear to be in cases in which choledochoduodenostomy had been performed without the use of a rubber tube. This operation was possible in 16 cases in which there was a long segment of common duct of ample diameter to enable the surgeon to effect an anastomosis.

Transplantation of an external biliary fistula was accomplished in 6 cases in this series. Three of the patients continued to have symptoms of biliary obstruction or cholangitis and 3 had died. However, we recall a patient who was free of obstructive symptoms 9 years after the transplanting, in 1926, of an external biliary fistula. He died from a cerebral hemorrhage 9 years after the operation.

COMMENT

Surgical trauma known or unsuspected accounts for nearly three-fourths of the benign strictures studied. Injury at operation does not occur necessarily because of the difficulty that one experiences with cholecystectomy, as very few of the patients had a history of acute inflammation of the gall

TABLE XI.—COMPLICATIONS AND DEATHS

Surgical procedure	Morbidity	Hospital deaths	Deaths after dismissal
Hepaticoduodenostomy	1 Cerebral accident	1 Hemorrhage	8 Hepatic insufficiency
	1 Pneumonia and empyema	1 Hepatic insufficiency	1 Hepatic abscess
	1 Pleural effusion	1 Peritonitis	4 Unknown
		1 Pneumonia	
Choledochoduodenostomy over a rubber tube	1 Cholangitis	1 Coronary occlusion	1 Adenocarcinoma of uterus
	1 Duodenal fistula	1 Bronchopneumonia	1 Operation elsewhere
	1 Peritonitis	1 Hemorrhage	1 Esophageal lesion
	2 Parotitis and pneumonia	1 Hepatic insufficiency	1 Ruptured spleen
			1 Unknown
Choledochoduodenostomy without a rubber tube	1 Cerebral accident	1 Uremia	1 Cardiac disease
			1 Hepatic insufficiency
Reconstruction of common duct over T tube	1 Bronchopneumonia	1 Hepatic insufficiency	1 Cerebral hemorrhage
		1 Hepatic abscess	1 Hepatic insufficiency
		1 Pyemia	1 Pneumonia
		1 Subdiaphragmatic abscess	2 Unknown
Transplantation of external biliary fistula	None	1 Hemorrhage	1 Hepatic abscess
			1 Unknown
Hepaticostomy	1 Atelectasis	5 Hepatic insufficiency	1 Hemorrhage
	1 Cardiac decompensation	1 Peritonitis	3 Hepatic insufficiency
	2 Cholangitis		
	1 Hemorrhage		
	1 Parotitis		
	1 Pneumothorax and pneumonia		
	1 Pneumonia		
Hepaticojejunostomy	None	None	2 Hepatic insufficiency
Choledochogastrostomy	None	1 Hemorrhage	None
Hepaticogastrostomy	None	1 Hemorrhage	None
Cysticoduodenostomy	None	None	None
Total	18	22	34
Per cent of 188 cases	10	12	18

bladder. Obesity is not an important factor, since the patients were found to vary in height and weight in approximately the range found in an average cross section of the population; actually a number of the patients were well below a normal weight.

The most important step in performing cholecystectomy is the individual identification and ligation of the cystic duct and artery. In doing this one avoids many pitfalls that lead to formation of stricture.

A number of strictures result from too close a ligation of the cystic duct, inadvertently unless the anatomy is clearly visualized, at its junction with the common duct. Ligation of the cystic duct at this point produces a constriction of the common duct with possible subsequent formation of stricture. In certain cases in which direct visualization is not obtained, it would not be difficult to put enough traction on the cystic duct to pull the common duct into a deformed U shape with application of the clamps across the U rather than across the cystic duct. This must have occurred in those cases in which segments of the common duct had been excised.

Many patients stated that their surgeon spoke of having had difficulty in managing a

hemorrhage during the course of the cholecystectomy. Here again, direct ligation of the cystic artery and duct will avoid this complication. If severe hemorrhage does result from a cystic artery that slips through a clamp, rather than blindly clamp into the region of the artery one can control the hemorrhage by digital compression of the hepatic artery in its course anterior to the foramen of Winslow and then seek the offending vessel and clamp it individually. In those cases in which there is severe inflammation with much edema and inflammatory change in the tissues one may find that the ligature will cut through the cystic artery. In such cases the hemostatic clamp can be left on, the incision can be closed about the clamp and the clamp can be loosened and removed in 4 or 5 days. Cholecystostomy may be the procedure of choice in these cases, cholecystectomy being performed at a later date.

The presence of anomalies in the biliary system as well as in the corresponding vessels makes the direct ligation of the cystic duct and artery imperative. Eisendrath in his classic study showed the frequency of abnormal relations. He found that 17 per cent of cystic ducts parallel the course of the common duct, occasionally to within 1 centimeter of the ampulla. The cystic duct spiraled about the hepatic duct in 8 per cent of the cases. The right hepatic artery may pass anterior, posterior or parallel to the cystic duct. The cystic artery may arise to the right or left or behind the common duct and may pass in front of it or behind it. The cystic artery is double in 12 per cent of the cases.

We believe that the extensive obliteration of the duct system, which in many cases extended into the intrahepatic ducts, can be attributed to chronic inflammation of the epithelium of the ducts. At least 12 per cent of the patients can be classified on such a basis. In one case known surgical trauma was followed by such an extensive obliteration of the bile ducts. This no doubt may explain the obliteration of the bile ducts in other cases even though they also presented external biliary fistula. In consideration of the possibility of this lesion resulting from rigorous curettage of the mucosa of the bile duct in performance of choledochotomy, we feel that particular care should be exercised in exploration of the common duct and that exploration of the common duct should not be carried out unless there exist definite indications for it. The chronic obliterative cholangitis which these patients present is due to a slowly progressive chronic inflammation that destroys the normal epithelium and leaves a scarred, contracted, nearly obliterated common duct.

We wish to emphasize that this group of patients do tolerate operation well and we believe that this fact should encourage surgical exploration in an attempt to re-establish the continuity of the biliary system, even in those cases in which the risk is considered to be grave. One is greatly impressed with this ability to undergo extensive operations, for these 188 patients underwent a total of 496 operations with only a 12 per cent mortality rate for the 188 procedures which we are studying. Two hundred and fifty-seven of these operations had been performed elsewhere. The ability of the liver to maintain a satisfactory function after years of constant injury is manifested by the 4 patients who suffered from symptoms of cholangitis for 10 to 12 years but were still alive at the time of the latest report.

Nearly a half of the patients who were well, 2 to 12 years after their reconstructive operation, had suffered from symptoms of biliary dysfunction which had subsided entirely. We would stress this fact in any evaluation of patients who return after a reconstructive operation for further management. Although many of these patients had chills, fever, jaundice and an enlarged tender liver at one time, they later became free from symptoms. One such patient after choledochoduodenostomy had suffered from symptoms of cholangitis for 2 years but had been entirely free of symptoms for 7 years at the time of the latest report. Apparently cholangitis is the factor present in these cases rather than a mechanical obstruction. Patients who have cholangitis improve when treated with sulfonamide drugs and when simultaneously the rate of flow of bile is increased by use of bile salts and increased ingestion of fluids. One can be aided in de-

termining the degree of mechanical obstruction by use of duodenal intubation in discovering whether bile is flowing into the duodenum in satisfactory amounts. If it becomes evident that one is dealing with a mechanically malfunctioning anastomosis, then re-exploration is indicated if the condition of the patient warrants further surgical treatment.

One probably obtains the poorest results in all surgery from attempts at reconstruction of the biliary duct system. However, when one considers the hopelessness of the situation without surgical intervention, the results can be viewed much more optimistically. Thirty-six per cent of all the patients were well 2 years or more after the reconstructive operation and a total of 67 per cent were alive. Of the 31 per cent who had symptoms of cholangitis and obstruction that persisted, a half required further attempts at reconstruction.

Actually in certain selected cases, reconstruction operations can be very satisfactory. If injury or severance of a common duct is recognized immediately and repaired, the ultimate result is quite satisfactory. Too, when there remains a long segment of common duct and the diameter is sufficient to enable the surgeon to do choledochoduodenostomy without the use of a Mayo-Sullivan tube or catheter, the results are gratifying. Sixty-two per cent of these patients were well 2 to 12 years after operation and less than a third of the 62 per cent had had temporary symptoms of cholangitis. If one elects to use a catheter or tube in performing choledochoduodenostomy, the results may be only slightly less gratifying according to our study, in which 55 per cent were living and well 2 to 12 years after the operation. When a T tube reconstruction was used the results proved only two-thirds as good as when choledochoduodenostomy was performed without a tube. Why this is true is not entirely apparent; it may be that removal of the T tube causes injury to the anastomoses and allows subsequent stricturing.

When the common duct is destroyed and one is compelled to use the hepatic duct in performing hepaticoduodenostomy, the results are the least favorable of all the reconstructions. Only 28 per cent of the patients were alive and well 2 to 12 years later.

It is surprising to discover that 4 (21 per cent) of the patients who underwent hepaticostomy in which an external biliary fistula was established were entirely well and without biliary drainage. A spontaneous internal fistula developed, and the patients gave a history of discharge of food particles for a time prior to closure of the external fistula. Therefore, if one is compelled by necessity to resort to hepaticostomy when an external biliary duct is not identified, all hope should not be abandoned. In one case in which there was a permanent external biliary fistula, a visit at the clinic 4 years later revealed the patient to be in relatively good health and able to perform her duties. She takes her own bile by mouth and her intake of calcium is high. A high intake of calcium must be maintained to prevent osteoporosis, which develops in patients who lose the biliary excretion.

Progress has been made in the management of a complication that has arisen in the evolution of biliary surgery. The place that the vitallium prosthesis will come to occupy remains to be ascertained. However, we wish to reiterate that the best treatment for benign stricture of the bile ducts is prevention, which can result only by impressing the seriousness of the problem on surgeons and by their adherence to rigid care in actual identification of the structures that they are handling when performing biliary operations.

SUMMARY

Benign stricture of the bile ducts is a tragedy for the patient and for the surgeon. In nearly three-fourths of the cases such a tragedy might well have been averted. However, there are certain strictures, at least 12 per cent in this study, which can best be explained on the basis of low-grade chronic inflammation, so called chronic obliterative cholangitis.

Although surgical results are far from being all that can be hoped for, nevertheless, surgical treatment does offer a real hope in certain types of stricture, for after choledochoduodenostomy 55 to 62 per cent of the patients

made satisfactory recoveries. If cholangitis and obstructive symptoms develop after a reconstruction operation, one would best defer further surgical treatment unless definite complete obstruction is proved, as nearly a half of the patients who were reported well 2 to 12 years after operation had experienced transient cholangitis and symptoms of obstruction at one time.

On the other hand surgical treatment should not be withheld from patients on the grounds of a poor risk, for these 188 patients who underwent 496 operations, 257 elsewhere, underwent 188 procedures with only a 12 per cent surgical mortality rate.

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THE REPAIR OF NASAL DEFECTS WITH THE MEDIAN FOREHEAD FLAP

Primary Closure of Forehead Wound

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THE purpose of this paper is to present a series of cases with nasal defects which have been repaired by vertical flaps from the median portions of the forehead. The classic Indian method of rhinoplastic procedure has many advantages over other methods which may be enumerated as follows:

1. The skin of the forehead when it is transposed over the nose to cover a defect harmonizes very well with the skin of the rest of the face.

2. The abundant blood supply makes it possible to utilize the tissue without creating a delayed flap.

3. Because the forehead is in such close proximity to the nose, the operative procedure is more simple as compared with other methods.

One great objection to the use of the forehead flap has been the resulting secondary deformity in the form of scars over the forehead. This serious drawback has forced plastic surgeons to resort to other methods, such as the use of a flap from the arm, a tube flap from a distant area (5), the Gordon New "sickle flap" (3), and many other procedures (2).

The utilization of a vertical flap from the median section of the forehead is not a new procedure; in fact, the original Indian method employed the median flap. Many surgeons, among them Schimmelbusch, Lexer, and others have used it. It seems, however, that only Schimmelbusch (4) considered the idea of closing the forehead wound by rotating two broad flaps from the forehead tissue, thus leaving eventually only a linear scar line on the forehead (1).

For many years I have utilized a vertical flap from the median section of the forehead to repair various types of defects of the nose. At first this method was used only for small defects of the nose, until it was gradually realized that large defects could be repaired by the same method.

Briefly, the technique consists of making two parallel incisions over the forehead, from one half to one inch apart, extending from the hairline to just above the frontal eminence on both sides. This flap is raised from its bed and when it reaches the region of the eyebrows, blunt dissection is carried downward almost to the root of the nose, thus saving the frontal vessels from injury.

The flap is then employed as a means of supplying tissue to repair the defect of the nose. The details of the repair will be described in connection with the case histories.

The defect of the forehead is closed immediately by approximating the edges of the forehead wound; the resulting vertical scar in the center of the forehead is a surprisingly inconspicuous line. Of course there is an upper limit to the size of the flap that can be taken from the forehead with a closure of the donor area by simple approximation of the borders of the wound. The size of the forehead and the degree of elasticity of the skin also have a bearing on the use of this method. Patients with low hair lines do not supply much tissue for the repair of a large defect. It is also apparent that the skin of the forehead in young people is more difficult to stretch, while in older patients the skin is usually quite lax and the borders of a forehead wound are more easily approximated.

However, with all these limitations in mind, I am satisfied that even though the forehead tissue is not as elastic as the tissues of other parts of the face, large gaps may be closed with approximation of the borders by the following methods:

1. In small gaps about one-half inch wide, there is no difficulty in bringing the edges

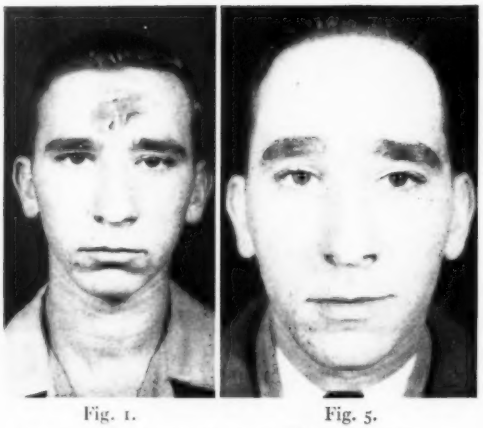

Fig. 1. Fig. 5.

Fig. 1. Hairy pigmented nevus before operation.
Fig. 5. Postoperative result after excision of birthmark.

Fig. 6.

Fig. 6. Extensive scarring with lack of development due to radium treatment of a birthmark in childhood.

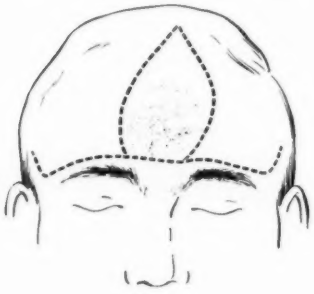

Fig. 2.

Fig. 2. The dotted line represents the incision at operation.

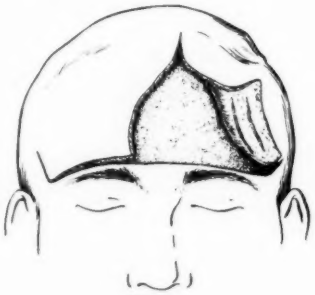

Fig. 3.

Fig. 3. The nevus has been excised, and the forehead skin is being stretched by vertical incisions through fascia and part of fat.

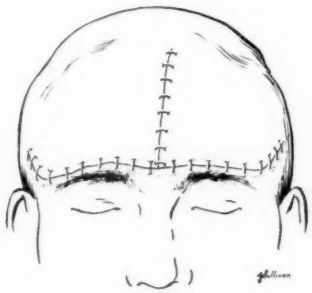

Fig. 4.

Fig. 4. The edges of the wound are approximated.

Fig. 7. Fig. 8.

Fig. 7. Scarred area excised and filled with median flap from forehead.
Fig. 8. Postoperative result.

Fig. 9.

Fig. 10.

Fig. 9. Nasal defect 2 months after the patient was bitten by a dog.
Fig. 10. Median forehead flap swung down and attached at tip of nose.

together with a median suture line after the forehead tissues have been undermined on either side of the gap.

2. If the forehead defect covers an area larger than one half inch, the skin is freely undermined on each side of the raw area. Then one or two incisions are made under the undermined skin, parallel to the incised edges, through the fascia but without penetrating all of the subcutaneous fat or any of the skin. This procedure will tend to loosen the skin of the forehead and will allow the approximation of the borders of the wound without undue tension.

3. In more extensive gaps, where a large, conspicuous birthmark was excised (Fig. 2), the borders of the resulting gap were approximated by (a) undermining freely, (b) by vertical cuts through the frontal fascia, and (c) by a horizontal incision just above each eyebrow which allowed for shifting of the skin toward the median line without distortion of the eyebrows.

From experience in a series of 25 cases, I have found that the median scar line over the forehead becomes very inconspicuous in most, while in other cases where a flap more than one inch wide was used, the resulting scar line may be visible but not deforming.

The types of nasal deformities which may be corrected by median frontal flaps cover a wide range:

1. Defects of the skin over the dorsum of the nose where a full thickness skin graft from behind the ear is not indicated because of the amount of tissue lost, such as is seen following excision of malignant growth. Grafts from

Fig. 11.

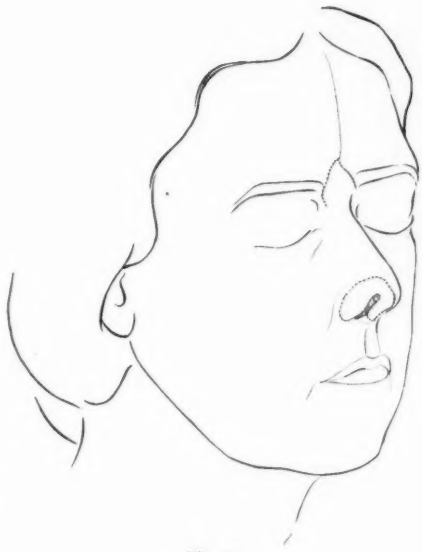

Fig. 12.

Fig. 13.

Fig. 11. Diagram showing method of turning flap on itself and attaching it distally to the lower part of the nose.

Fig. 12. New ala and part of tip and columella made from the forehead flap, part of which has been sutured back in place between the eyebrows.

Fig. 13. Postoperative appearance.

behind the ear are also not indicated in areas where there is lack of blood supply due to radiation.

2. Short, stubby noses where elongation of the tip requires additional skin.

3. Defects of the nasal tip, borders of nostrils, and columella, which can be corrected by judicious planning and manipulation of the median frontal flap.

4. Large defects involving the lower half of the nose.

5. Defects of the side of the face where a large perforation has resulted following operation for removal of a malignant tumor.

Fig. 14. Extensive scarring and lupus erythematosis of nose.

Fig. 15. Median forehead flap attached to defect created by excision of abnormal skin.

From the variety of cases listed, it is seen that median flaps have been utilized for all types of defects except the restoration of total loss of the nose. When one analyzes the various defects of the nose resulting from trauma or from malignant lesions, it is realized that total loss of the nose is a rare occurrence.

Careful planning is essential for the utilization of the forehead flap. If the flap is intended to supply a skin covering alone, one is often obliged to shift the flap and spread it over the defect in different stages. Where the inner lining of the nose is missing with loss of tissue about the tip and side of the nose, it is often necessary to use a full thickness graft under the raw area of the flap, and after it "takes" to transpose it to the area of the defect. At other times if the area of the lost inner lining is small, a skin graft may be sutured to the raw surface of the flap and transposed to the new position in the same operation. In large defects involving the inner lining, such as defects over the entire dorsum, defects of the nostrils, or defects of the side of the face with openings into the maxillary sinus, it is possible to extend the flap and have the skin of the forehead form the inner surface of the nose or sinus. Then the borders are sutured to the mucous membrane edges of the defect, and a full thickness graft is put over the raw superficial surface of the flap. Later, at the proper time, the proximal end of the flap is cut through and the perforation at the upper end of the defect is closed.

In those cases in which large flaps have to be used and in which the resulting midline forehead scar becomes conspicuous, the scar later can be excised and resutured.

One difficulty when large flaps are required is that hair-bearing skin may have to be taken with the flap. This later can be rectified in several ways. The two most convenient which have been used in this series are (a) excision of the hairy area if it is small with simple approximation of the borders of the defect thus created, and (b) lifting up the hairy portion and trimming away the hair follicles so that future hair growth may be prevented.

Fig. 16. Postoperative result. The patient had put on considerable weight.

Fig. 17. Appearance when first seen. The defect is due to excision of cancer of the nose.

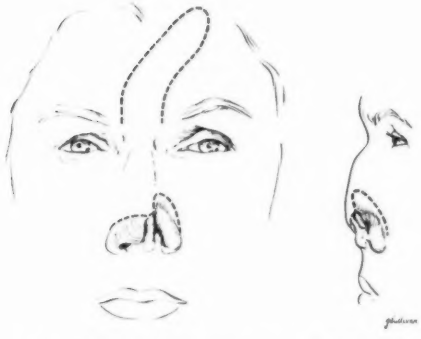

Fig. 18. Dotted lines represent the incisions made.

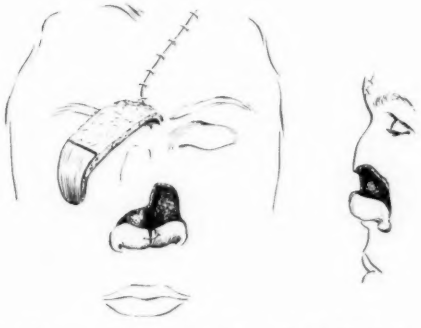

Fig. 19, right. New alae sutured together in midline. On the patient's left side the defect is complete; on the right side mucosa is present. The forehead flap is not entirely a midline flap. The distal end of the flap has a skin graft applied.

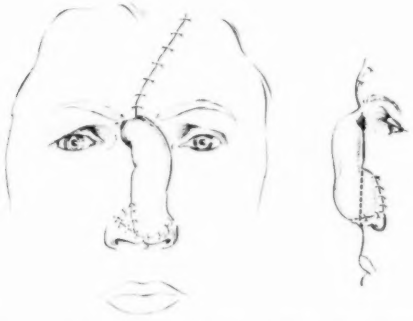

Fig. 20. A small triangular skin graft has been sutured over the defect on the right side. The skin lined flap fills the complete defect. The dotted line represents the line of incision allowing the flap later to be pulled farther down, making a tip and columella.

Fig. 21. Same as Figure 20.

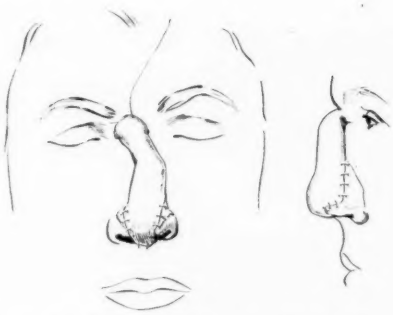

Fig. 22. The flap attached farther down, thus creating a more normal tip and columella.

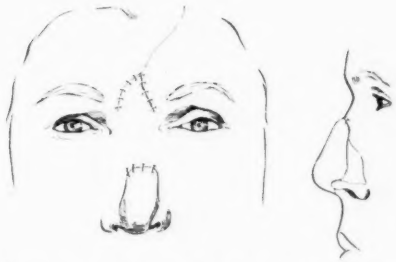

Fig. 23. Proximal portion of flap divided and sutured back in place between the eyebrows.

Fig. 24. Final result of Case 5.

The following cases are selected because each demonstrates minor variations of the technique here described. Several of these patients are still undergoing plastic procedures; and, therefore, cannot be considered completed, but are shown here to emphasize the modifications which this method makes possible.

CASE 1. H. O., aged 17 years. This patient had a birthmark about 2 inches in diameter in the center of the forehead. The nevus was sharply outlined, slightly raised, hairy, and dark brown in color (Fig. 1).

July 6, 1943. Operation was performed under local anesthesia. The nevus was excised, including one-fourth inch of normal skin around the periphery of the birthmark. The resulting defect was closed in the following manner. A triangular piece of scalp was removed mostly from the hair bearing area (Fig. 2). Next the forehead skin including the temporal region was freely undermined on each side of the raw area. Horizontal incisions were made just above the eyebrows and at the distal ends these incisions were carried upward for about 1 inch (Fig. 3). In order to gain further relaxation of the frontal flap, two vertical incisions were made through the fascia into the fatty layer, care being taken not to make the incisions too close to the skin. Thus, the two frontal flaps were advanced forward and sutured at the median line (Fig. 4). A pressure bandage was applied.

The final result was quite satisfactory and the resulting scar line was practically inconspicuous (Fig. 5).

CASE 2. F. R., aged 17 years. This patient had a birthmark over the nose, which was treated with radium in childhood. The birthmark disappeared but the treatment resulted in a conspicuous scar, and the nose failed to develop (Fig. 6).

May 3, 1941, examination showed an oval shaped, adherent scar covering the greater part of the dorsum of the nose. The nose was small in size and saddle shaped. There was no intranasal pathology. June 28, 1941, operation was performed under novocain anesthesia. The scar over the dorsum of the nose was removed, and to repair the resulting defect a median vertical flap from the forehead was utilized. This flap was a little over one-half inch

Fig. 25.

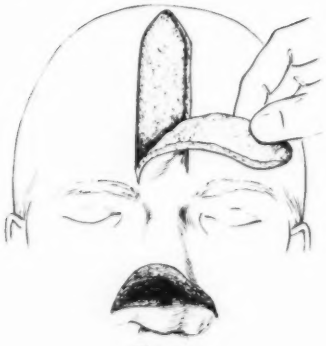

Fig. 26.

Fig. 25. Loss of lower part of nose; etiology uncertain.
Fig. 26. Lower part of nose swung down as a double ended flap to make the new alar borders. Median forehead flap elevated.
Fig. 27. a and b, median forehead flap filling superficial part of defect created when the double ended flap was swung down.

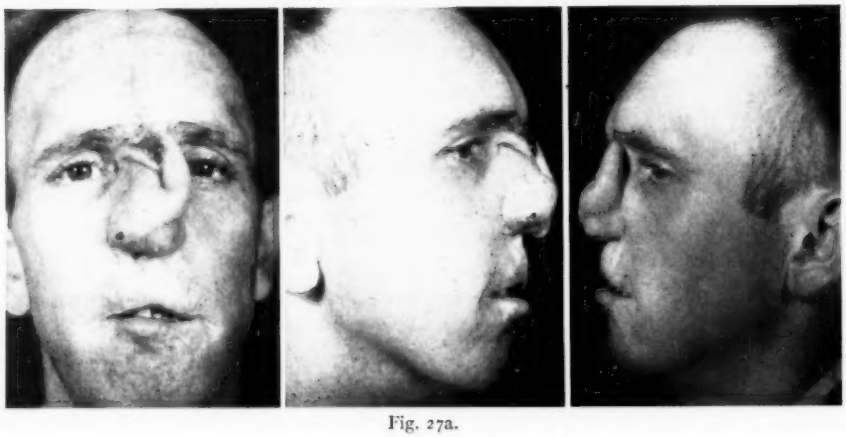

Fig. 27a.

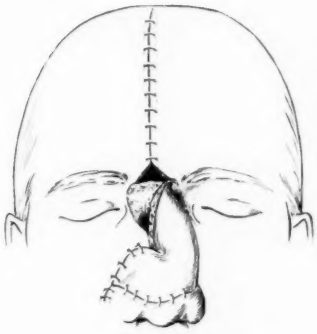

Fig. 27b.

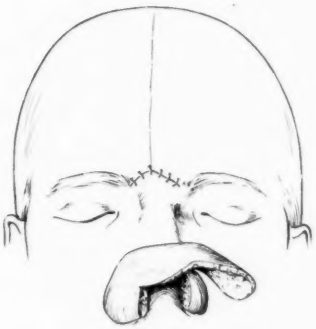

Fig. 28.

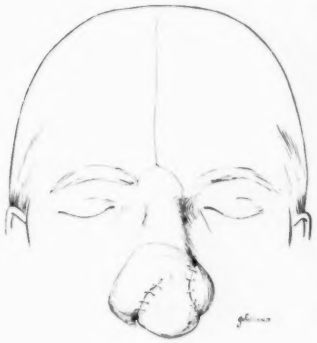

Fig. 29a.

Fig. 28. Alae separated and this defect filled with proximal end of forehead flap.

Fig. 29. a and b, Middle portion of forehead flap sutured on each side to the new alae. The end of the flap folded in to form the inner surface of the nose.

Fig. 30. Bone graft inserted, considerable fat removed.

wide and extended from the hair line to the glabella. The flap was brought down, rotated upon itself, and then sutured over the defect. The forehead wound was closed by approximating the wound edges.

July 15, 1941, operation was performed under novocain anesthesia. The unused part of the flap was cut through and part of it was returned to its original position between the eyebrows. The remaining part was shaved of its epithelial layer and inserted underneath the attached portion of the skin flap, thus providing bulk to the dorsum of the nose (Fig. 7).

July 22, 1942, the appearance of the nose was greatly improved (Fig. 8). The median line scar was hardly visible.

CASE 3. H.P., aged 56 years. This patient gave a history of having had the tip of her nose bitten by a dog on September 1, 1942. She was seen 2 months later. Examination at that time showed that the nasal tip, the greater part of the right nostril, and the upper part of the columella were missing. The contracted scars had caused considerable distortion about the tip of the nose and the nostrils (Fig. 9).

December 9, 1942, operation was done under novocain anesthesia. A long, vertical flap on the forehead about one-half inch wide was raised, twisted upon itself, brought down, and sutured over the columella and the tip of the nose. It was possible to approximate the borders of the forehead wound except for a small area between the eyebrows (Figs. 10, 11).

January 7, 1943, operation was done under novocain anesthesia. The pedicle flap extending down from the forehead was cut through about one-half

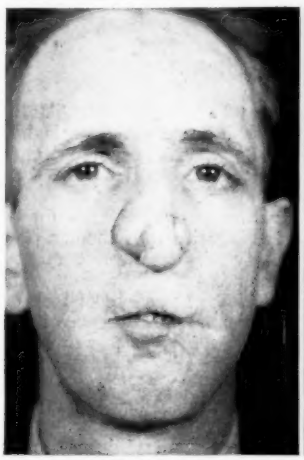

Fig. 29b.

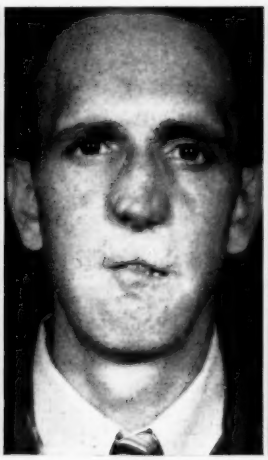

Fig. 30.

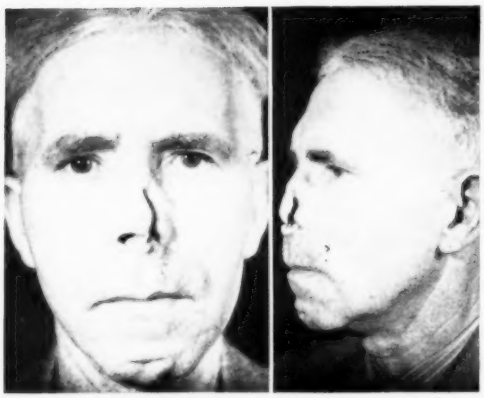

Fig. 31.

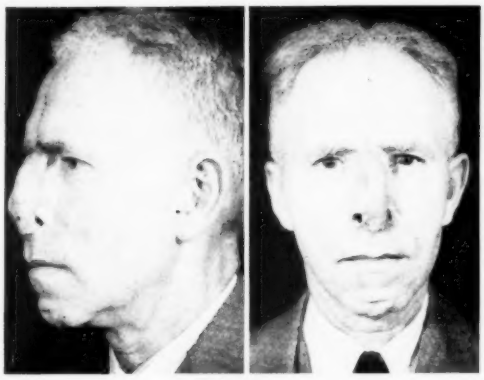

Fig. 34.

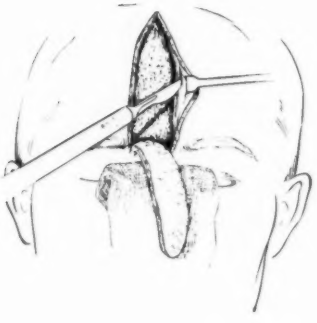

Fig. 32a.

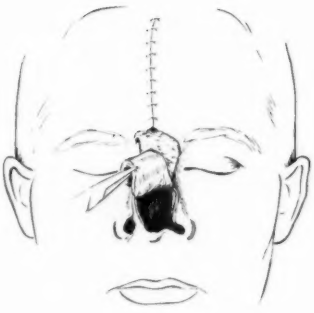

Fig. 32b.

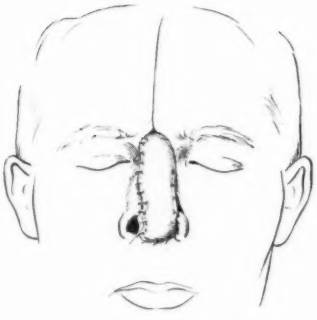

Fig. 33.

Fig. 31. Nasal defect following excision of adenocarcinoma.

Fig. 32. a, Median forehead flap being elevated and relaxing incisions in frontal fascia. b, Flap turned over and sutured to make inner lining of nose.

Fig. 33. Full thickness graft sutured on back of flap to make outer lining.

Fig. 34. Same as Figure 33.

inch below its proximal base. The upper part was trimmed and sutured into its original position over the frontal eminence. The lower part of the pedicle was brought down and sutured to the side of the right nostril (before suturing, it was necessary to free the retracted part of the right nostril in order to let it assume a normal position, Fig. 12).

May 4, 1943, operation was done under novocain anesthesia. A small tongue-shaped flap was placed on the right side of the nose from the columella area. An incision was then made in the indented margin of the right ala and the columella flap was rotated into position there. A fair amount of cartilage was taken from the tip of the septum shortening the nose and improving the contour (Fig. 13).

Case 4. A. W., aged 43 years. The past history revealed that the skin of her nose had not been normal since the age of 23 years. Various forms of medical treatment had not helped. The condition was diagnosed as lupus erythematosis by several physicians including those at the skin department of the Massachusetts General Hospital. Because of sensitivity to gold and bismuth therapy the usual medical treatment was not available for her. The thickened, red skin, with its follicular plugs, gave the nose a "warty" appearance. On October 22, 1943, the affected areas of skin were excised, but the excision proved difficult because of lack of subcutaneous fat with increased adherence of the skin to subcutaneous structures. The raw areas were covered with full thickness grafts obtained from both postaural regions. The "take" of these grafts was poor, but eventually, the raw areas granulated and epithelialized.

I first saw this patient on July 24, 1944, and in view of her past history, decided to operate, utiliz-

Fig. 35.

Fig. 39.

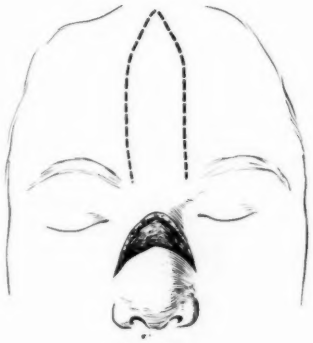

Fig. 36.

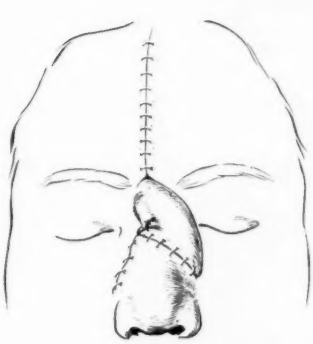

Fig. 37.

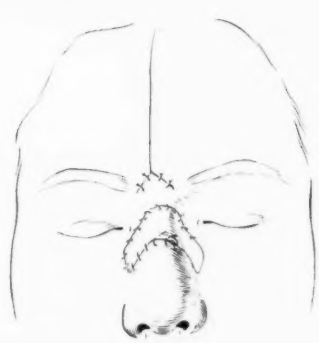

Fig. 38.

Fig. 35. Nasal deformity which was the result of repeated sepsis.

Fig. 36. Entire skin and cartilage of lower nose freed up and swung down. Median forehead flap outlined.

Fig. 37. Flap filling defect on left side of nose.

Fig. 38. Nasal defect on left side filled by proximal part of median forehead flap.

Fig. 39. Final result in Case 8.

ing a vertical flap from the forehead for the repair of the nose (Fig. 14).

November 30, 1944, operation was done under local anesthesia. All of the scarred tissue was excised, and a vertical forehead flap about 1 inch wide was brought down and sutured over the raw area. It was possible to close the donor area on the forehead by freely undermining the skin on each side of the wound and by making vertical incisions through the under surface of the flaps (Fig. 15).

December 19, 1944, operation was performed under local anesthesia. After severing the flap near its proximal end, the upper portion was returned to its former position between the eyebrows. The remaining part of the flap was folded down to cover an an area on the right side of the nose near the border of the nostrils where the original disease existed.

April 13, 1945, operation was performed under local anesthesia. An area which showed return of lupus on the right side of the nose was excised. This resulted in a triangular space about one third of an inch in diameter on the side of the nose. In order to close it a rectangular flap was raised from the side of the nose and sutured in position. The columella was thinned by making an "L" shaped incision following the original scar line and removing the excessive fatty tissue. The borders were then sutured together. The scar over the frontal eminence was excised, and the borders of the wound approximated (Fig. 16).

Case 5. W. MacN., aged 50 years. This patient had had an excision of the lower part of the nose in June, 1943, for cancer. Examination one and one-half years later showed loss of the lower part of the

nose including the tip. As shown, parts of each ala were present. There was no evidence of recurrence (Fig. 17).

April 1, 1944, under local anesthesia, the alae were freed up, swung down, and sutured together in the midline. This maneuver left a defect which on the right side had for its base submucosa and mucosa, and which on the left side was complete, there being no lining of the nose present (Fig. 18, 19). A skin graft was put over the part of the defect with mucosa present but the complete defect required a double lined flap made by sewing a skin graft on a flap from near the midline of the forehead (Fig. 20, 21).

May 13, 1944, under local anesthesia, the distal end of the flap was extended down from its attachment at the lower part of the nose by first freeing it and by then suturing it in a lower relationship to the alae. This created a new columella (Fig. 22).

June 12, 1944, that portion of the flap not used in the repair was returned to its place on the forehead after it was severed from the portion filling the former nasal defect (Figs. 23, 24). Redundant tissue was excised from the latter part of the flap thus improving the contour of the nose. Local infiltration with novocain and adrenalin was used.

Case 6. R. S., aged 27 years. This patient, June 22, 1944, gave a history of having had cancer which destroyed the lower part of the nose. There had been no recurrence in 8 years. The history was rather vague, and the condition might have been lupus vulgaris or a luetic infection. Examination showed that the lower half of the nose had been destroyed. The upper lip was extensively scarred but the scar tissue was soft. The outline of the mouth was somewhat distorted (Fig. 25).

November 8, 1944, operation was performed under local anesthesia. Two parallel vertical incisions were made over the center of the forehead, about 1 inch apart, running from the hair bearing area down to the eyebrows. The borders of the forehead wound were approximated in a straight line. Next an incision was made about one-half inch from the lower border of the nose, cutting through the skin as well as the mucous membrane, thus exposing the nasal cavity. This double ended flap was brought downward to form the borders of the nares (Fig. 26). A large piece of skin was removed from behind the right ear, carefully trimmed, and sutured to the inner surface of the nose to fill the gap in mucosa created by the former step. The forehead flap was then brought down and sutured between the two halves of the nose to fill the defect and also to cover the full thickness skin graft that had been sutured to form the inner surface (Fig. 27, a,b). The nasal cavity was packed and a pressure bandage was applied externally.

December 7, 1944, operation was done under local anesthesia. The scar between the eyebrows was excised. A median incision was made at the tip of the nose and the two halves of the lower border were separated (Fig. 28). The middle portion of the forehead flap was sutured on each side to the new alae while the end of the flap was folded in to form the inner surface of the nose (Fig. 29, a,b). This spread the lower part of the nose and gave more room for breathing. Enough surface tissue was left at the tip of the nose to form a columella at a later date.

February 14, 1945, operation was done under local anesthesia. The lower half of the nose was trimmed to make it a little thinner. In so doing, it was found that the hairy section on the right side of the nose could be excised (the hairy portion had been the upper part of the forehead flap). An incision was made across the tip of the nose and a considerable amount of fat was removed from the bulbous area.

July 13, 1945, operation was done under local anesthesia. A bone graft from the right iliac crest was imbedded subcutaneously over the dorsum of the nose (Fig. 30).

This patient is not reported as a completed case but is described here to show another way of using the median forehead flap; i.e., turning its skin surface inward to make the inner lining of the nose and using a graft to provide the exterior covering.

Case 7. T. M., aged 63 years. The patient presented himself with the defect shown in Figure 31 following the excision of an adenocarcinoma of the nose on July 26, 1944.

March 30, 1945, operation was done under local anesthesia. A median forehead flap three-fourths of an inch wide was elevated and the edges of the defect thus created were approximated in the midline. Next the scars were excised along the borders of the defect of the nose and the skin along these borders was separated from the mucous membrane below. The median forehead flap was turned over, the skin facing the inside of the nose, and was sutured first to the columella and then to the mucous membrane on each side of the gap (Fig. 32a, b). A large full thickness skin graft was removed from behind the ear and was sutured over the now exterior denuded area on the forehead flap. The nasal cavity was then packed (Figs. 33 and 34).

May 25, 1945, operation was performed under local anesthesia. After the upper attachment of the flap was cut, the skin from the frontal eminence was put back in position, occupying a triangular space between the eyebrows. The subcutaneous fat tissue between the two skin layers of the flap was completely separated from the outer layer of the skin through the opening at the top of the nose. This subcutaneous fat was pulled toward the tip of nose and held in the tunneled area in order to give more fullness to the tip. The excess skin was excised and a small perforation of the middle part of the dorsum of the nose was closed. A pressure bandage was applied.

This case is still under treatment.

CASE 8. M. M., aged 28 years. As a result of a nasal fracture in 1922 and numerous plastic procedures including bone grafts, this patient presented herself with a short nose, the result of a marked loss of skin, bone, and cartilage from repeated attacks of sepsis (Fig. 35).

February 2, 1942, operation was done under local anesthesia. Bilateral vestibular incisions were made and the skin was elevated from the underlying nasal structures. The columella was then incised at its attachment at the lip. An inverted "V" incision was made with its arms running laterally downward from the dorsum to the sides of the nose. The entire lower part of the nose was then pulled downward (Fig. 36) leaving a defect which on the left side was corrected by a median forehead flap swung down and sutured at the left side of the nose (Fig. 37). The midline forehead gap thus produced was then closed with No. 0000 kaldermic sutures. The right side of the nasal defect was closed by reapproximating the skin edges in their former position.

February 14, 1942, operation was done under local anesthesia. The scar left from the operation on February 2, 1942, was excised on the right side and the tissues freed so that the right side of the nose could be brought down as far as the left. This produced a defect which was filled by severing the base of the forehead flap and suturing it to the right side of the nose. That portion of the flap not used in the repair was replaced between the eyebrows (Fig. 38).

June 29, 1942, operation was done under ether anesthesia. A bone graft was taken from the ilium. An incision was next made anterior to each nostril at the tip of the nose and connected to a midline incision in the columella. The nasal tissues were undermined and the carefully shaped bone graft was inserted into the cavity. The original incision was closed by interrupted kaldermic sutures.

October 17, 1942, operation was done under local anesthesia. An incision was made across the bridge of the nose externally along the line of junction of the upper portion of the skin graft with the nasal skin. The flap was undermined and thinned down. Then with a hand rasp the bone graft was smoothed and the incision sutured with No. 0000 kaldermic sutures (Fig. 39).

SUMMARY

A method of repair of defects of the nose and adjacent cheeks, utilizing a median flap from the forehead, is presented. It has distinct advantages over many of the other types of rhinoplastic repair. Several cases are also described which illustrate various modifications of the fundamental technique.

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THE SURGICAL TREATMENT OF ACUTE CHOLECYSTITIS

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With Introductory Remarks by GEORGE J. HEUER, M.D., F.A.C.S.

IT was, I think, in 1910 or early 1911 that a private patient of Dr. Halsted was admitted to the Johns Hopkins Hospital with symptoms and signs of acute cholecystitis. I saw the patient with Dr. Halsted. He decided to operate; and so soon as the patient was properly prepared she was taken to the operating room. I assisted Dr. Halsted at the operation.

The gall bladder was large and acutely inflamed, and the omentum was loosely adherent to it. Without hesitation and without comment to indicate that he was doing something unusual, he proceeded to do a cholecystectomy. It was the first cholecystectomy I had seen for acute cholecystitis. I was struck by the smooth convalescence of the patient, and the case made a great impression upon me.

At the time, cholecystostomy with drainage was practically the universal treatment for gall-stone disease of the gall bladder; and the deliberate attack upon the gall bladder in the acute phase of acute cholecystitis was rare indeed. When in 1922 I went to Cincinnati, I found again that operation for acute cholecystitis was not practiced, the acute process being allowed to subside; and if and when it did subside, cholecystostomy was commonly done although cholecystectomy was being discussed and practiced.

I had a good opportunity in Cincinnati to observe the course of acute cholecystitis under a waiting policy. I have to admit that I observed the gall bladder perforate while the patient was in the hospital, and that I saw not only extracholecystic localized abscess but generalized peritonitis supervene. I also observed that the gall bladder in acute cholecystitis may proceed in its pathological course to gangrene and perforation in the presence of subsiding and minimal signs and symptoms. Such observations led me to operate more frequently and to encourage my resident staff to operate in the acute phase of the disease; and before I left Cincinnati to come to New York I had decided that early operation in acute cholecystitis was the surgical treatment of choice.

Early operation in this disease was then established by me as a policy to be followed by my staff on my ward service at the New York Hospital, and it has consistently been followed since September, 1932. Dr. Glenn will tell you the results of such a consistent policy.

OVER a period of 13 years, from September 1, 1932 to September 1, 1945, a total of 527 patients with acute cholecystitis have been operated upon in the New York Hospital. There were 13 deaths—a mortality rate of 2.4 per cent. It is the purpose of this discussion to present our definition of the surgical treatment of acute cholecystitis and to elaborate in some detail upon the operative procedures that are commonly employed. In the discussion of these operations the indications and contraindications for each procedure are reviewed and the resulting complications discussed.

By the surgical treatment of acute cholecystitis we mean operating upon the patient when adequately prepared unless there is some contraindication that is not immediately reparable. The gall bladder was removed in 460 patients, or 87.4 per cent, of those subjected to operation, and cholecystostomy was performed in 67 cases, or 12.6 per cent. The

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Presented at the New York Academy of Medicine, February 1, 1946.

TABLE I.—ACUTE CHOLECYSTITIS NEW YORK HOSPITAL—SEPTEMBER 1, 1932 TO SEPTEMBER 1, 1945

Total cases	527
Deaths	13
Mortality, per cent	2.46
Operative Procedures	
Cholecystectomy	460
Cholecystostomy	67*
Common duct exploration	43

*12.6% of total operations.

TABLE II.—ACUTE CHOLECYSTITIS, NEW YORK HOSPITAL, SEPTEMBER 1, 1932 TO SEPTEMBER 1, 1945—PATIENTS FIFTY YEARS OF AGE OR OVER

Total	175
Deaths	9
Mortality, per cent	5.4
Operative Procedures	
Cholecystectomy	140
Cholecystostomy	35*
Common duct exploration	22

*20% of total operation.

additional procedure of exploration of the common duct was limited to those in which indications were definite, and these totaled 47, or 8.9 per cent. The policy has been adhered to that the welfare of the patient is continually to be kept in mind and that the operative procedure employed is to be that which promises the greatest possible benefit and least hazard. The operation is not decided upon entirely before the procedure is undertaken. For instance, if during operation cholecystostomy seems to be the procedure of choice, cholecystectomy is abandoned.

Cholecystostomy was performed in 67 instances and was followed by 5 deaths. This procedure is clearly indicated when the patient is too ill to withstand cholecystectomy or when cholecystectomy presents too great difficulties. For the extremely debilitated patient or for the very ill, we doubt if there are any contraindications for cholecystostomy. It may be done under local anesthesia, disturbing the patient very little; and it may be a life-saving operation. The decompression of the biliary tract averts catastrophe by preventing progressive liver damage if complete biliary obstruction is present.

In determining the type of operation to be done, the gross appearance of the presenting pathological changes is of importance. In the first place, if there is gangrene and perforation with accompanying generalized peritonitis, simple drainage of the abdomen together with cholecystostomy is indicated. If there is gangrene and perforation which has resulted in localized peritonitis or abscess in the region of the extrahepatic portion of the gall bladder, then one may choose between cholecystectomy and cholecystostomy. However, in the presence of extensive adhesions of the omentum to the gall bladder and into the biliary fossa, it is indeed questionable whether these should be disturbed and a cholecystectomy done. If the patient is unusually ill and if postoperative complications appear in the offing, then certainly cholecystectomy should not be attempted. Perforation of the gall bladder with a small abscess or perforation into the adjacent liver tissue is no contraindication to cholecystectomy. The patients with simple acute cholecystitis are in general best treated by cholecystectomy.

Common duct exploration in acute cholecystitis has been limited in our clinic to those patients with unequivocal indications for common duct obstruction. If these exist, common duct exploration should be undertaken even though it adds additional risk to the procedure. The incidence of postoperative complications is in this series apparently increased. At the same time it may be said that these patients are usually in the group that is more seriously ill. For the extremely ill, jaundiced patients, decompression (that is, cholecystostomy) may be utilized as a compromise procedure, having in mind, of course, following the subsidence of jaundice, the exploration of the common duct with the patient in a greatly improved condition.

The presence of jaundice requires the determination of blood prothrombin and the evaluation of any bleeding tendency, and, in the presence of acute disease, time may not be afforded for this. For such patients the use of whole blood transfusions and parenteral administration of vitamin K may prevent serious postoperative hemorrhage.

The common duct was explored in 47 of the patients in this series, an incidence of 8.9 per cent. Stones were recovered in 29 of these, or 61.7 per cent. It is probable that the opening

TABLE III.—ACUTE CHOLECYSTITIS, NEW YORK HOSPITAL, SEPTEMBER 1, 1932 TO SEPTEMBER 1, 1945—PATIENTS UNDER FIFTY YEARS OF AGE

Total	352
Deaths	4
Mortality, per cent	1.13
Operative Procedures	
Cholecystectomy	320
Cholecystostomy	32*
Common duct exploration	25

*9% of total operations.

of the common duct in the patient without stones does not materially increase the postoperative complications. On the other hand, failure to remove common duct stones may lead to catastrophe. Therefore, when the surgeon is unable to conclude definitely whether or not there are stones, it may be better judgment to open the common duct.

The operation of choice in acute cholecystitis is cholecystectomy. The removal of the gall bladder interrupts the pathologic process and averts the danger of gangrene and perforation. This procedure is sometimes contraindicated because of: (1) The presence of peritonitis due to perforation of the gall bladder. In this situation an extensive operation is contraindicated because of the gravity of the patient's condition. (2) Conditions which make it difficult to identify the important structures in the biliary fossa. When the gall bladder is greatly distended and adherent, the adjacent viscera may be so distorted that anatomic relationships are obscured. In this situation there is danger of inadvertently injuring the hepatic vessels or the common duct. (3) The presence of jaundice caused by obstruction in the common duct may be a contraindication to an extensive operative procedure. It is usually better to drain the gall bladder and thereby relieve the jaundice than to subject the patient to removal of the stone from the common duct. (4) In a patient whose general condition is so grave that a general anesthetic and prolonged operation are not justified. This state of affairs is likely to arise when the cholecystitis is superimposed upon systemic disorders, such as hypertension or cardiovascular and renal disease. In such cases a compromise must be sought in the form of surgical treatment which, without adding to his burden, tides the patient over the immediate crisis.

In the series of 527 patients treated surgically, 175 were 50 years of age or over. There were 9 deaths, or a mortality rate of 5.14 per cent. One hundred and forty patients were subjected to cholecystectomy; 35, or 20 per cent of the 175, were treated by cholecystostomy. Twenty-two had, in addition to these operations, exploration of the common duct. The mortality rate of 5.14 per cent in patients who were 50 years of age and over indicates the definitely greater risk to which they are exposed; for in all patients less than 50 years of age the mortality rate following operation was 1.13 per cent. The following chart with an analysis of the 9 deaths shows the complications which terminated fatally (see Table IV).

In the consideration of the group of deaths it may be of significance that all but one were women, and the duration of known biliary tract disease was of long standing—longer, in our opinion, than the histories recorded. Furthermore, the duration of the immediate attack was of 2 days or more with one exception. Jaundice was marked in 5 of the patients.

In patients 50 years of age and over, acute cholecystitis is a more serious disease than it is in the younger age group. The mortality rate is almost five times as great in this series. It has been our experience that changes in the vascular system, i.e., arteriosclerosis, hypertension and diabetes, are greater in those who have biliary disease than in a corresponding number of individuals of the same age group without it. Cowdry in a volume regarding arteriosclerosis places the incidence of arteriosclerosis in the general population at 25.6 per cent for those between 50 and 60, and 38 per cent for those over 60. McCallum found that patients over 50 dying as a result of biliary tract disease associated with gall stones showed an incidence of arteriosclerosis of 68 per cent. The trend of our population toward the older age groups indicates that we may anticipate an increasing number of these geriatrical problems unless they can be reduced by preventive surgery. For biliary tract disease it means operating in the earlier

TABLE IV.—SUMMARY OF DEATHS AFTER OPERATION

Case	Sex Age	History of biliary disease in years	Duration of attack	Jaundice	Findings	Operation	Cause of death
1	F 66	8 plus	3 days	Yes	Acute cholecystitis with perforation, peritonitis	Cholecystectomy with drainage	Peritonitis
2	F 67	4 plus	7 days	No	Acute cholecystitis with gangrene	Cholecystostomy	Peritonitis, bacteremia
3	F 50	20 plus	10 days	Yes	Acute cholecystitis, cholelithiasis, common duct obstruction	Cholecystostomy	Bacteremia, stone in common duct, thrombosis hepatic artery
4	M 72	7 plus	8 days	Yes	Acute cholecystitis, cholelithiasis	Cholecystostomy	Hepatic failure, biliary cirrhosis
5	F 57	Inadequate history	4 days	No	Acute cholecystitis, cholelithiasis	Cholecystectomy, drainage abscess	Subhepatic abscess*
6	F 70	12 plus	8 hours	No	Acute cholecystitis, cholelithiasis	Cholecystectomy	Coronary occlusion, cardiac failure.
7	F 64	2 plus	2 days	Yes	Acute cholecystitis	Cholecystectomy with drainage	Adrenal insufficiency
8	F 54	4 plus	3 days	Yes	Acute cholecystitis, common duct obstruction	Cholecystectomy, common duct exploration	Leakage from cystic duct, subphrenic abscess, pancreatic necrosis
9	F 72	?	3 days	No	Acute cholecystitis, carcinoma of cecum	Cholecystectomy, Ileocolostomy	Intestinal obstruction, hypertensive cardiac disease

*No autopsy

decades when acute cholecystitis represents an early phase of the disease. If our contention is correct, a deleterious effect upon the vascular system may be interrupted.

The remaining 352 of the 527 patients were under 50 years of age. There were 4 deaths, a mortality rate of 1.13 per cent. Three hundred and twenty, or 90.9 per cent, were subjected to cholecystectomy and 32, or 9.1 per cent, were treated by cholecystostomy. Only 25, or 7.1 per cent, had in addition to one of the above procedures exploration of the common duct. This is a far more favorable outcome than our experience with the group of patients who were 50 years or over.

Table V is self-explanatory and emphasizes in each death that the biliary disease was of long standing. This suggests that acute cholecystitis is but a phase of the disease.

Given a patient with a definitely established diagnosis of acute cholecystitis, our policy provides for his or her surgical treatment as soon as adequate preoperative preparation has been carried out. There is no undue haste and no neglect in this preparation; and it is, of course, not undertaken in patients in whom operation is contraindicated. It may require several hours to prepare these patients; no step should be neglected. A surgical operation on the biliary tract is to each patient a serious procedure, never to be entered upon lightly, and those with acute cholecystitis are certainly no exception. Once prepared, the operation should be undertaken

TABLE V.—SUMMARY OF DEATHS AFTER OPERATION—UNDER FIFTY YEARS OF AGE

Case	Sex Age	History of biliary disease in years	Duration of attack	Jaundice	Findings	Operation	Cause of death
1	M 41	5	1 day	Yes	Acute cholecystitis	Cholecystectomy	Cardiac and renal failure, liver death
2	F 49	15	3 days	Yes	Acute cholecystitis	Cholecystectomy	Subdiaphragmatic abscess, peritonitis
3	F 49	12	2 days	No	Acute cholecystitis, stones in common duct, acute pancreatitis	Cholecystectomy Choledochotomy	Pulmonary emboli* 27th postoperative day
4	M 44	4	10 days	No	Acute cholecystitis	Cholecystectomy	Hypertension, cardiorenal failure

*No autopsy

and the nature of the procedure and the extent determined by the findings and the general condition of the patient.

How different is this from the so called conservative attack which considers these patients a medical problem, leaves them in their homes where complications may develop and be unrecognized. There can be little disagreement that in a well regulated hospital the constant observation and care of a patient will be far more efficient than in the home, where the patient may be seen once a day by the physician. I need not remind you that laboratory data, temperature records, and personal observation by more than one individual are of great value in determining the course of events in any pathological process.

It is the duty of the surgeons to present this viewpoint to the general practitioner and to demonstrate that such a policy will diminish the deaths due to this particular disease.

I feel that in the heat of argument there have been radical claims made by those who favor early operation and those who are opposed to it. Those in favor often insist that operation be done within a period of hours without dwelling long on preoperative preparation, and this certainly is not sound. On the other hand, those opposed to operation assume the policy that surgery is not indicated and that it should not be carried out, and they cite figures based not upon the early surgical treatment of acute cholecystitis but upon treatment of the complications that arise from these cases.

In conclusion, it should be reiterated that successful surgery is dependent upon every detail associated with it, and the patient with acute cholecystitis is no exception. Preoperative and postoperative care and meticulous surgery are necessary to support the policy that we maintain.

CONCLUSIONS

1. The surgical treatment of acute cholecystitis can be accomplished with a mortality rate comparable with that of nonacute biliary tract disease.

2. Acute cholecystitis is a more serious disease in those who are 50 years of age or older.

3. Cholecystostomy can frequently be used in the seriously ill to tide them over an episode that would go on to irreversible complications or in those who might not survive a more formidable surgical procedure such as cholecystectomy.

4. Exploration of the common duct should be undertaken in the presence of acute cholecystitis only when there are clear-cut indications.

5. A policy that provides for the surgical treatment of acute cholecystitis and places him in a hospital should be to the best interest of the patient.

OBSERVATIONS ON A CONCEPT OF INGUINAL HERNIA REPAIR

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THERE is once more a rising tide of speculation among surgeons as to the actual results of the traditional methods of inguinal hernia repair. There is coincidental reflection of dissatisfaction with such results in the continuing publication of alternative methods of radical revision of the abdominal wall. Statistics are usually furnished in an effort to show that fewer failures have occurred with the recommended technique than in any other series cited by their author from the literature. There is nothing novel about this situation, for in an exceedingly interesting article, to which further reference will be made, Pitzman stated in 1921: "The size and endlessness of the stream of inguinal herniotomy technique raises the strong suspicion that something is fundamentally wrong."

At the time of going on active duty in the Medical Corps, the present writer had a concept of inguinal hernia, which though by no means original, was unorthodox. A rather concentrated experience with this disorder in naval personnel has strengthened his belief in the validity of this concept and in the necessity of including certain technical steps in any plan for achieving correction. It has been impressive to observe the development of a similar point of view among many thoughtful surgeons who, entering service with a more traditional concept of inguinal hernia, have also had the opportunity of daily exploration or observation in this field. In the 20 month period between February 15, 1944, and October 15, 1945, 1,398 operations were done for primary inguinal hernia, 89 operations for recurrent inguinal hernia, and 11 operations for femoral hernia at the United States Naval Hospital, Naval Training Center, Great Lakes, Illinois. Due to the exigencies of the service, tabulation of the operative findings has not been completed, but reference will be made in this paper to observations on which those of us who had duty there during that period are in agreement. Sliding hernia will be excluded from consideration.

A critical review of the literature for the last 10 years leaves the writer with one conviction which is very disappointing (his own position as unorthodox having been stated): there is no published evidence that in any group of patients with inguinal hernia operated on by the Bassini technique (including such variations in the disposal of the external oblique aponeurosis as are usual), there would have been fewer failures had another operative procedure been chosen! This conclusion is derived from the fact that no standards of reporting have been agreed on. The converse of the first conclusion is that there is no statistical evidence that a surgeon advocating one of the suggested alternatives to the Bassini would have had poorer results had he used the latter. The fact is that far more complete data are available as to the results of operations done by the Bassini method than of any, including that advocated by the writer, intended to supplant it. Those who may question these assertions will find their answer when they seek to apply to the published statistics of any given procedure the best facts available as to the relationship between the intervals (in years) after operation and the percentages of recurrences. Burdick and Shelley (16, 17, 18) in analyzing their own recurrences detected in yearly follow-up examinations, found that in 284 and 210 traced recurrences, respectively, less than one-half were found in the first year and approximately two-thirds in the first 2 years; about 83 per cent were detected in the first 5 years in each series and the remainder thereafter. It happened that the overwhelming majority of pa-

The views expressed herein are those of the author and are not to be construed as those of the Bureau of Medicine and Surgery or of the Navy Department.

Read before the Western Surgical Association, November 30, 1945.

tients in these large groups were operated upon by the Bassini method. The writer does not know of any statistical follow-up report for a series of cases done by techniques other than the Bassini (as previously defined) furnishing data to which these principles can be applied.

The traditional view of inguinal hernia has it that there are two types, indirect and direct, and that this hard-and-fast compartmentation is maintained throughout the life of the hernia. It notes the increasing frequency of direct hernia with advancing age and muscular relaxation, considers diverticular hernia through Hesselbach's triangle to be rare and conceives the ratio of direct to indirect hernia as being about 1 to 5 in adult males. Those surgeons who, like the writer, believe the results of the Bassini repair to be worse than necessary, although we cannot yet prove that our preferred methods have given better, find much recently recorded evidence that the conception of inguinal hernia just outlined gives a very limited and, in some respects, a false view of the situation. The unusually comprehensive findings of Skinner and Duncan of the United States Public Health Service record that, of 1126 primary inguinal hernias, there were 426 with indirect sacs plus varying degrees of weakness, relaxation, or virtual absence of the posterior wall below the internal ring and 700 direct hernias, including 308 bilocular (i.e., combined) hernias; "few" patients were found to have simple, indirect sacs without enlargement of the aponeuroticofascial margins of the internal ring. Ramos and Burton of the Veterans' Administration, report that the majority of 457 primary inguinal hernias were bilocular. The significance of these findings as to the complexity of the "average" primary hernia in the adult male lies in the fact that their series are the only ones large enough to have statistical significance in which is reported routine exploration for secondary sacs, for thickness and state of tension of the posterior wall, and for the accurate estimation of the size of the internal ring by the introduction of a finger through the opened neck of the sac at the internal ring. This procedure was recommended by Hoguet in 1920, by Pitzman in 1921, and more recently by Fallis, Zimmerman, and Harkins, with whose views on the anatomical problems to be met the writer entirely concurs. The series of anatomical papers by Anson and McVay and their later collaborators, beginning in 1937, are unquestionably the most notable anatomical contribution to the subject of hernia to come from the dissecting room in many years. Their pertinent findings in a very large series of dissections are that the inguinal ligament does not receive insertions of the cremasteric portion of the internal oblique or of the transversus aponeurosis and that the inguinal ligament itself is attached only loosely in its midportion to the fascia lata of the thigh. They urged that since the normal insertion of the transversalis fascia is to Cooper's ligament along the superior ramus of the pubis, laxness of the lower portion of the posterior wall should be remedied by suture of the transversalis fascia (and such fibrous elements of the lowest portion of the internal oblique as might be present) not to the inguinal ligament, but to Cooper's ligament. They also point out that the so-called conjoined tendon of the internal oblique aponeurosis and transversalis fascia is a very inconstant structure. The first clinical application of their findings was in the repair of direct hernia but their warning against the use of the inguinal ligament in any part of its course has been extended to the entire field of inguinal hernia repair.

Data on one further, very important technical aspect of the operative treatment of hernia are those furnished by Parsons which present the results of two comparable series of hernias operated on during the same period by the same group, the only difference in technique being that fine silk was used for ligatures and sutures in one series, catgut (size and characteristics unknown) in another. In 458 operations for inguinal hernias of all types in which silk was employed, the recurrence rate was 3.5 per cent; in 244 operations utilizing catgut, the rate of failures was 12.7 per cent. His figures can be tabulated to show that in the 91 cases most likely to failure of the silk series (combined, sliding and recurrent hernias) the recurrence rate was less than 8 per cent in each category, whereas of 49

similar cases closed with catgut, the rate of failure was above 20 per cent for each group. Although there are objections to accepting Parson's figures as being truly indicative of the ultimate rates of failure (all were done by a modified Bassini technique), yet the superior performance of silk over catgut can be accepted without reservation in one respect and with considerable reservation in another. That the recurrence rate followed the rate of wound infection (with approximately a ratio of 1 to 3 in favor of silk) throughout all his cases is clear. But since the length of time in which confinement to bed after operation was enforced is not alluded to, the influence of this factor in wound healing of his cases is not known. It is notoriously true that wounds sutured with catgut, however fine, heal more slowly than when silk is employed and those of us who used fine catgut extensively in the past were quite aware that in wounds whose anatomic and physiologic characteristics made them liable to separation under stress, it was necessary to enforce recumbency for a longer period before a firm scar was obtained than would have been the case with silk. This is, in the view of the surgeon familiar with the processes of wound healing, elementary in the postoperative management of the patient whose wound is sutured only with catgut. No data on the occurrence of herniation through any operative incision having the characteristics described are complete without a clear statement of the duration of strict confinement to bed in a position of semirecumbency. This realization seems to be missing from much surgical thought today and will require emphasis in the current trend to early ambulation. Shelley (16, 17, 18) found that in 1110 repairs of primary indirect inguinal hernia without postoperative complications, in whom the postoperative hospital stay (not confinement to bed) was for the 11 to 15 days, customary in that institution, recurrences occurred in 7 per cent of the patients. A group of 336 patients with similar operations were confined to the hospital for 16 days or more because it was feared that they might develop complications, yet in them there were only 4.5 per cent of failures! Only catgut was used in either series.

Let us enumerate and comment on those steps which the writer regards as being essential to the performance of a radical hernioplasty with the smallest risk of failure. It is to be understood that the posterior wall of the inguinal canal is not merely the portion of Hesselbach's triangle between the inferior margin of the internal ring and the pubis, but also extends upward along the medial and lateral margins of the internal ring to its uppermost aspect; in patients with indirect hernia, the ring is invariably enlarged beyond the accepted normal dimensions, once its aponeuroticofascial margins have been demonstrated. This has been the observation of the writer in over 160 personally operated upon inguinal hernias on Naval personnel, of whom almost all had an indirect factor so far as the sac is concerned.

There are three major objectives of operation: (1) exploration of the components of the hernia (the sac, its contents and the abdominal wall of the inguinal region); (2) excision of the sac, whatever its characteristics, and closure of the peritoneum; (3) such plastic revision of the abdominal wall as may be indicated (complete or limited). Performance of the following steps will facilitate the accomplishment of these objectives.

1. Mobilization of the cremaster from its uppermost insertions into the transversus aponeurosis at the lateral margin of the internal ring and from its origins in the internal oblique muscle about the superior and medial margins of the external ring. Excision of these highest fibers of the cremaster exposes the medial and lateral margins of the internal ring, defines the free margin of the internal oblique muscle which is then retracted superiorly to expose the entire cord bundle and indirect sac in their passage through the internal ring. Excision of this portion of the cremaster also reduces the size of the cord bundle in the portion of its length which is to be brought out of the internal ring in closure and assures fascia-to-fascia approximation of the margins of the transversus aponeurosis. An intact cremaster is the greatest obstacle to identification of the transversus aponeurosis (or to realization of its existence as a readily accessible structure) known to the writer.

2. Opening the peritoneum at the internal ring and immediate exploration of the peritoneum and wall with an assay of the strength and thickness of the posterior portion of the wall below the inferior margin of the internal ring. This has been elaborated on previously. If any weakness of the posterior wall in Hesselbach's triangle is found, the peritoneum should be dissected out down to the bladder, the latter freed from the peritoneal attachment and the redundant peritoneum excised along with proximal portion of the indirect sac itself. A good case can be made for routinely carrying out this excision of the peritoneum to the bladder. The writer does not dissect out the portion of the (indirect) sac distal to its point of division unless its extension along the cord is very short indeed. Taking a wedge-shaped section out of the anterior aspect of the distal portion of the sac is adequate guarantee against the occurrence of hydrocele of the cord, were any needed. The peritoneum should be opened for exploration in the case of a diffuse bulge of the entire posterior wall unless it has been opened through the region of the internal ring. Failure to do so will result too often in overlooking a direct sac of diverticular type.

3. If the lower portion of the posterior wall is found to be weak, the remaining portion of the cremaster should be excised promptly. This will assure more accurate definition of the aponeuroticofascial structures about Hesselbach's triangle and will assure fascia-to-fascia approximation throughout the wound. Pitzman made it clear in 1921 that there was confusion as to the indirect origin of many apparently direct sacs. As the internal ring continues to be dilated by the increasing contents of an indirect sac, its lower margin eventually reaches the pubis and a "direct" sac, for all practical purposes, then exists.

4. Properitoneal fat, especially in the vicinity of a direct sac, should be mobilized and excised. This step decreases the "wedge" effect of the tissues immediately behind the newly closed wall and facilitates the accurate identification of the medial and lateral aponeuroticofascial margins of the entire posterior wall. It importantly diminishes the gap across which the deep layer, as well as more superficial ones, must be approximated in full-length ("complete," as the writer prefers to term it) revision of the abdominal wall, in which the cord is always transferred to the subcutaneous fat and the inguinal canal obliterated.

5. Closure of the posterior wall is further facilitated by accurately gauging the thickness of the medial margin throughout its length with a finger inside the peritoneum before closure of the latter. Two or more Allis forceps grasp the transversalis fascia and whatever fibrous elements are present in the inferior portion of the internal oblique at the inferior angle, next to the pubis, and at intervals extending superiorly along the medial leaf, keeping the muscular portion of the internal oblique elevated off of the underlying aponeurosis and transversalis fascia. Lateral traction on the Allis forceps will be of aid during closure of the medial leaf to the corresponding structures of the *lateral leaf* (transversalis fascia inferiorly, transversus aponeurosis superiorly) *of the posterior wall*. The writer has rarely failed to demonstrate this lateral layer, which lies obviously medial to the inguinal ligament, if the latter is carefully cleaned. Not uncommonly they blend almost indistinguishably. A continuous suture of doubled, fine (No. 000) chromic catgut enables the tension to be distributed evenly. The tension is notably slighter than if approximation of the medial leaf to the inguinal ligament is attempted, for the gap to the latter structure is wider. By the use of a continuous suture, extrusions of properitoneal fat into this all-important suture line are avoided. The most inferior suture is put through the medial leaf, then through the fibrous and ligamentous tissues along the ramus of the pubis, including the periosteum and Cooper's ligament. It is the writer's assumption that the anterior fascial layer of the femoral sheath is often caught by the sutures in the lateral leaf of transversalis fascia at a higher level. This suture is continued upward and locked at intervals until, with a narrow retractor forcing the cord into the upper angle of the internal ring, the fascial margins of the latter have been closed deep to the cord. Interrupted mattress sutures of No. 40 cotton are then placed at intervals of

about one-half inch throughout the length of this layer. This, as performed by the writer since 1942, is almost exactly the method of placing the first layer of sutures advocated by Skinner and Duncan. The anatomical advantages of closing the internal ring deep to the cord and transferring the latter to the upper angle seem obvious.

6. The free margin of the sheath of the internal oblique muscle is then re-attached to the transversus aponeurosis adjacent to the inguinal ligament with cotton sutures, starting at the superior angle of the wound, and proceeding inferiorly only as far as one can go without tension. This brings the free margin of the internal oblique muscle well below the level of the *newly* reconstituted internal ring in every case.

7. The medial and lateral leaves of the external oblique aponeurosis have usually been stretched somewhat by a hernia of any size, permitting imbrication across the lower portion of the previous suture line without tension, deep to the cord. The medial leaf is usually brought across first, the lowest suture again being placed through all structures down to the pubis. These leaves are imbricated under only the slightest tension with cotton sutures as far superiorly as possible, the cord again being retracted superiorly and laterally in an oblique plane through all fascial layers. The imbricated external oblique aponeurosis is sutured to the underlying deep layer in the lower inch of the closure.

8. The *transfer* of the cord to the fat, with obliteration of the inguinal canal, has been described. The writer has tried to persuade his colleagues and his students for years of the incorrectness of the usual phrase "transplant" of the cord, and will persist in an apparently hopeless effort at accurate descriptive terminology. It is, perhaps, of interest that all the steps in the "complete" (full-length) revision, or plastic repair, of the wall, with the exception of the avoidance of the inguinal ligament in closure and the routine opening of the peritoneum in monolocular direct hernia, were part of the routine radical operation for inguinal hernia as performed by Willard Bartlett, Sr., in 1928 when the writer joined his father in the private practice of surgery.

A case can be made for the "limited" operation in which the transperitoneal exploration reveals only moderate dilatation of the internal ring (to less than half the total length of the posterior wall) and a firm lower portion. The writer sees no advantage to be gained by obliteration of the inguinal canal in such instances. High division and suture of the sac, excision of the upper portion of the cremaster muscle as described, and approximation of the margins of the internal ring behind the cord deal thoroughly with the situation at this simple stage. The mobilized internal oblique is replaced and closure in anatomical layers completes the operation. This procedure should supplant the Ferguson operation entirely, as it avoids damage to the internal oblique muscle, accurately diminishes the size of the internal ring and thereby restores the posterior wall at its point of weakness under these circumstances, which the Ferguson does not do. On the basis of his experiences in the service, and of the anatomical data referred to, the writer would expect this "limited" plastic repair to be the procedure of choice in nearly 50 per cent of adult males under 30 years of age, with far less frequency in patients above that age and in practically all children.

SUMMARY

There is a wide difference between the traditional conception of inguinal hernia and that which is currently postulated on the basis of recent clinical and anatomical observation. The resemblance is slight between Bassini's ideal of "the rebuilding of the hernial canal, as this exists under physiological conditions, that is, a canal with two openings, an abdominal and a subcutaneous, further, with two walls, a front and a back, through the middle of which the spermatic cord would run obliquely"—and our adoption of all available means to obliterate the canal. We know that we cannot bring the transversus and the internal oblique muscles to the inguinal ligament and make them stay there and we suspect that we damage them in making the attempt. We are confident that the margins of the transversus aponeurosis and of the transversalis fascia cannot be accurately de-

fined or adequately approximated by his method, which does not include exploration of the sac and wall from within the peritoneum and excision of the cremaster muscle.

CONCLUSION

1. Bassini will always be honored as the pioneer in the establishment of (1) opening and high ligation of the hernial sac and (2) of radical revision of the relationship of the spermatic cord to the musculoaponeurotic structures of the abdominal wall as essential steps in the repair of inguinal hernia.

2. His operation will not be abandoned until evidence is produced that alternative methods have regularly yielded lower percentages of failure.

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THE GASTRIC DIGESTION OF LIVING TISSUE

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ALTHOUGH the digestion of dead animal tissue ingested as food is well understood, the digestion of living tissue, especially autogenous tissue, remains obscure. Why the stomach does not digest itself during life is a question that has never been answered satisfactorily. John Hunter postulated a "vital principle" in all living tissues which prevents digestion, but the presence or nature of such a "principle" has not been demonstrated. Obviously different tissues vary in their ability to withstand the corrosive action of gastric juice. Secretions which are quite innocuous in the healthy stomach may simply irritate the walls of a gastric fistula but cause painful erosions of the skin at the mouth of the fistula. The question of autodigestion has long interested physicians, partly as a matter of scientific curiosity, but chiefly because it is related intimately to such clinical problems as the pathogenesis and healing of peptic ulcer, the violent peritonitis which follows acute perforation, perforations which invade the pancreas or liver, anastomotic jejunal ulcer, gastrocolic fistula, and the destructive effects in the lungs of aspirated gastric contents.

Claude Bernard in 1859 showed that the leg of a live frog thrust through a fistula into a dog's stomach is soon digested away. The same is true of a rabbit's ear (8). Observers have not been in agreement, however, regarding the digestion of experimental autoplastic grafts. Katzenstein, Kathe, Best, and others claimed that living spleen, intestine and omentum implanted in a dog's stomach are digested, but opposite results were obtained by Holtz, Licini, and Tietze (6). Mann and others (2, 6, 7) have shown that patch transplants of jejunum, so placed that only the mucosa of the intestine is exposed to gastric contents, remain unchanged for long periods of time (as long as 1½ years) unless they are situated at the lesser curvature, in which case ulcers often develop in the grafts.

A more detailed study of autodigestion was made by Dragstedt and his associates (3, 4). These investigators reported that the intact spleen, kidney, and pancreas implanted in openings in the anterior wall of the stomach or duodenum of dogs are not digested even after several weeks, and they concluded that these living organs resist the digestive action of normal gastric and duodenal contents. Patch transplants of small intestine were found to be digested, however, by the pure secretions of an isolated stomach or a Pavlov pouch. So also was the spleen. It was observed, furthermore, that intestinal loops implanted with the serosal surface exposed to gastric juice undergo partial digestion with the formation of smooth round perforations. Dragstedt and his coworkers decided that the outer layers of the intestinal wall are less resistant than the mucosa to the digestive action of gastric juice.

The present investigation has extended those observations. Our early experiments showed that small windows in the normal canine stomach heal so rapidly that the digestive effects of gastric juice are masked by the processes of repair; consequently, in most of our experiments large openings were made through which tissues or organs were deeply implanted in the lumen of the stomach, thus insuring prolonged full exposure to gastric contents. Special pains were taken to preserve normal or adequate blood supply in the tissues tested.

About 135 dogs were used in these experiments. Stock laboratory animals were employed, operations being done aseptically under pentobarbital sodium anesthesia. Fine cotton thread was used for ligatures and sutures. Water and food (dog pellets) were permitted freely after operation. The animals were explored surgically or were sacrificed after various intervals. Autopsies were per-

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Aided by grants from the Doctors' Research Fund and the Rockefeller Third Research Fund of the University of Utah School of Medicine.

formed as soon as possible after death, blocks being cut for microscopic study.

Gastric acidity was measured in about half of our animals by taking single samples of fasting gastric contents at the time of implantation. No cases of anacidity or excessively high acidity were encountered. Animals retested at the time of exploratory operation showed no significant changes in acidity as the result of implantation of extraneous tissue in the stomach. Free acid varied from 8 to 57 units, the average being 24 units; combined acid varied from 8 to 61 units, with an average of 23 units; and total acid varied from 19 to 84 units, the average being 56 units. All the animals had been starved for 24 hours preoperatively; none had received histamine or other secretagogues. It may be said, therefore, that the degree of acidity in these experimental animals corresponded in general to that usually found in the fasting stomach of healthy humans.

EXPERIMENTS

1. *Digestion of living omentum.* Small holes in the gastric wall were covered with thick tongues of omentum (Fig. 1, A) and large holes with flat thin patches of omentum (Fig. 1, B). Under these conditions there appeared to be relatively little digestion of the omentum, even after as much as 2 months constant exposure to gastric juice. Microscopic examination showed a layer of granulation tissue at the gastric surface, with some superficial necrosis and débris formation; more deeply a dense fibrosis extended into the plug or patch.

However, when a large tongue of omentum was inserted through a window into the gastric lumen (Fig. 1, C), a different result was observed. After 3 days the implant appeared acutely inflamed, with superficial ulceration and necrosis, and in less than 3 weeks it had digested completely away. The erosion never extended farther than the level of the gastric wall. In prolonged experiments the site of implantation simply showed a shallow crater with gastric epithelium growing across the fibrosed omental base formed by the neck of the implant (Figs. 2 and 3).

It is possible, of course, in the experiment just described that the omental implant may have been strangled by contraction of the gastric window, thus rendering it more susceptible to digestion. Additional experiments were performed, therefore, in the attempt to insure good circulation in the implanted tissue. First, by means of a two or three stage operation, a tongue of omentum was threaded through an isolated segment of jejunum which was then fastened in the gastric window (Fig. 4). These implants were likewise digested within 2 weeks as far as the distal end of the jejunal segment. It was noted that the part of the intestine which had extended into the lumen of the stomach was also digested, thus leaving a smoothly healing junction of gastric and jejunal mucosa.

Experiments were performed also in which a tongue of omentum was implanted in the stomach after it was threaded in like manner through a short cuff of large bore rubber tubing. The rubber sewed to the gastric window effectively prevented the omentum from compression by the gastric wall. This operation was done in a single stage. Leakage was prevented by attaching omentum to the stomach around the tube. Three such preparations, examined after 6, 16, and 32 days, respectively, all showed complete digestion of the omentum as far as the distal end of the rubber tube.

In 2 dogs, a tongue of omentum was passed through a tunnel in the anterior abdominal wall so as to re-enter the abdominal cavity near the stomach. After 2 and 4 weeks, respectively, these preparations of omentum, which appeared perfectly normal were implanted in the stomach. To prevent constriction large windows were made in the stomach, and the margins of the openings were sutured to the anterior abdominal wall around but not touching the omental implants (Fig. 5). In this way we could be quite sure that omentum with unimpaired circulation was exposed to the action of gastric juice. One of the implants, examined by exploratory operation after 8 days, appeared dark red and felt hard. When the animal was sacrificed on the 16th day, this implant had digested away to the level of the abdominal wall. The second animal, sacrificed on the 14th day, likewise showed complete digestion of the implant as far as the

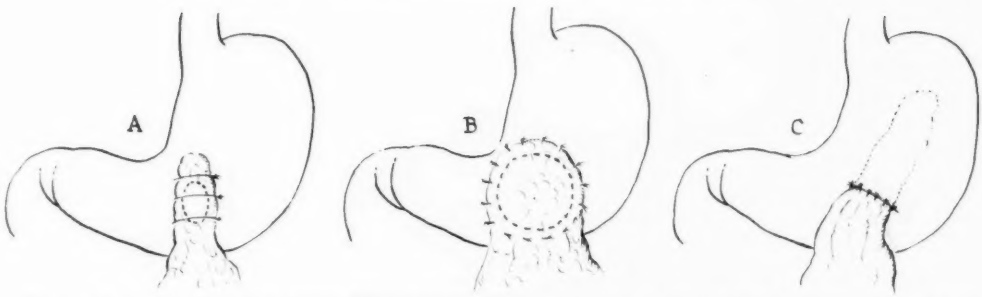

Fig. 1. Three methods used to expose living omentum to the action of gastric juice: A, a small oval window in the stomach covered with a tab of omentum; B, a large window covered with a thin patch of omentum; C. a large tongue of omentum inserted through a window into the lumen of the stomach.

abdominal wall. In both animals the omentum still embedded in the abdominal wall appeared perfectly normal on gross and microscopic examination.

Finally, small pieces of omentum were grafted on the serosal surface of the anterior gastric wall so as to receive their blood supply entirely from it. Some of these free grafts had the appearance of normal fatty omental tissue, while others were (by design) more or less fibrosed; but all were living and healthy. The transplants were subsequently turned into the lumen of the stomach on pedicle flaps of gastric wall (Fig. 6). In this way living omentum, having undergone various degrees of fibrosis, was exposed to gastric juice. In most instances these omental grafts were digested in from 6 to 18 days, although a small island of fat surrounded by fibrous tissue was found in one instance after 44 days. It was not determined whether the fibrous grafts were digested more or less rapidly than the more normal fatty tissue.

It may be concluded, therefore, that healthy living omentum is digested when deeply implanted in the stomach, but placed patch-like over a gastric window it becomes fibrosed and suffers only superficial digestion.

2. Digestion of living intestine. The digestion of part of an isolated segment of jejunum which protruded into the stomach has already been noted. In that experiment it was obvious that all the layers of the intestinal wall had undergone digestion, although the destructive process ceased abruptly at the level of the gastric wall (Fig. 4 B).

An isolated piece of jejunum with intact mesenteric blood supply was sewed patchlike in a gastric window so that only its mucosa was exposed to gastric juice (Fig. 7). This experiment has been done many times by earlier investigators and our results are similar to theirs. No changes were detected in this flat jejunal implant after as long as 262 days.

It was found, furthermore, that after a graft of this sort had "taken" its mesentery could be divided without injury to the patch. When, however, the jejunal transplant was invaginated into the gastric lumen (a) by infolding that part of the stomach with sutures, or (b) by turning in a pedicle flap of gastric wall including the transplant (as in Fig. 6), digestion of the jejunal mucosa occurred, although adjacent comparable gastric mucosa remained normal.

Intact loops of jejunum and ileum were also implanted in the stomach so as to expose the serous surface to gastric juice. When small windows were used, relatively little digestive action was observed and the gastric defects healed rapidly. When the loops were deeply implanted in large windows, however, (Fig. 8) perforation and digestion of the exposed intestinal wall regularly occurred. Areas of necrosis and perforation were observed as early as 2 days after implantation; after 11 days extensive necrosis and multiple perforations were found; after 27 days digestion of the exposed wall was nearly complete with formation of smooth gastrointestinal mucosal junction. Figures 9 and 10 show clearly one stage in that digestive process.

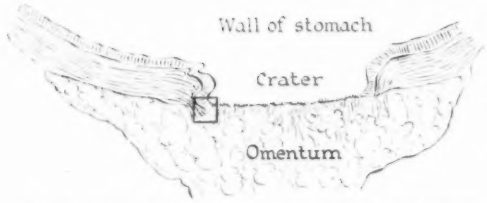

Fig. 2. Cross section of an omental implant after 21 days. All intruding tissue has been digested away leaving a shallow ulcer. The base is fibrotic with a little superficial necrosis. The margins show proliferation of gastric epithelium. The area within the square is shown in greater detail in Figure 3.

The canine appendix is relatively much larger in diameter than the human appendix. In 6 dogs the appendix was implanted so as to project into the lumen of the stomach. Twenty-four hours after implantation the serosal surface showed acute inflammatory reaction; after 6 days the entire wall was involved with inflammatory changes, hemorrhages, and necrosis; after 1 month the appendix had disappeared altogether, leaving a smooth, round, healthy-looking gastrocecal fistula.

Similar effects were observed after implantation of the cecum and colon (Fig. 11).

It appears, therefore, that the outer layers of the living intestinal wall are readily digested by normal gastric juice. Intact jejunal mucosa was not found to be digested, however, by normally acid chyme unless its supporting walls were first destroyed, impairing its blood supply, or unless it was invaginated into the lumen of the stomach.

3. Digestion of living organs. The long slender lobes of the canine liver lend themselves well to implantation in the stomach. The most accessible lobe, usually the left central one, was thrust as far as possible through a prepyloric window into the stomach. The lobe was then anchored in place with transfixing sutures and the omentum was drawn up and tucked around the edges of the window to prevent leakage of gastric contents. Care was taken not to constrict the lobe. After 4 days great thickening of the capsule had occurred, with superficial fibrosis and necrosis of the exposed liver, but beneath the surface the parenchyma was normal and the blood supply appeared to be undisturbed. By the end of 4 weeks the implanted lobe had been digested away to the level of the gastric window, leaving a shallow crater with superficially necrotic base (Figs. 12 and 13). In only 1 of 4 dogs observed for more than 26 days were there fibrosis and necrosis extending well into the unplanted portion of the lobe.

The gall bladder was implanted successfully in 5 dogs. This organ was first dissected partly or wholly free from the liver, the cystic vessels being left undisturbed. One-third to three-fourths of the viscus was then implanted through a window in the anterior gastric wall. We were careful not to puncture the gall bladder with anchoring sutures. The animals were sacrificed 6 to 11 days after operation. In every instance the implanted portion of the gall bladder had been digested. Two animals showed complete healing of the mucous margins and smoothly formed fistulas. The unimplanted portion of the gall bladder always appeared normal, showing that the blood supply of the organ as a whole had not been compromised by the operation.

The tail of the pancreas was satisfactorily implanted in the stomach in 3 dogs. Partial digestion was observed after 24 days (Fig. 14) and complete digestion to the level of the gastric stoma after 48 days.

Several attempts at deep implantation of the spleen failed because the organ slipped partly or entirely out of the window. Those cases showed only superficial necrosis and fibrosis of the exposed surface. In 3 dogs we succeeded in implanting about 4 centimeters of the inferior pole of the spleen, anchoring the organ securely with transfixing sutures. These animals, sacrificed on the 19th, 28th and 32nd days, all showed complete digestion of the implants as far as the level of the gastric stoma (Fig. 15).

Deep implantation of the kidney was technically difficult and a number of dogs were lost from leakage of gastric juice and resultant peritonitis. When the implant was made tangentially in a gastric window, only thickening, inflammation, and superficial necrosis of the capsule were noted (Fig. 16), a result previously described by Dragstedt. We eventually succeeded in 5 dogs in implanting the upper third of the left kidney without leakage of gastric contents. One animal died 3 days

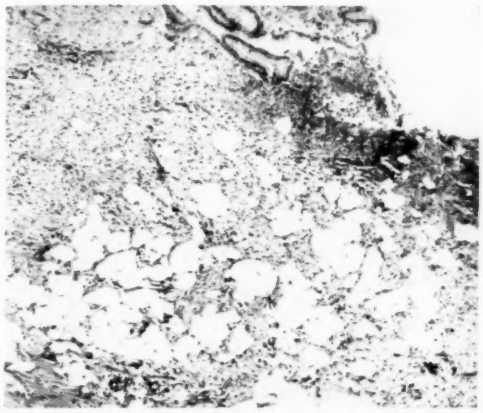

Fig. 3. Photomicrograph of an omental implant after 21 days, showing the edge of the residual crater illustrated in Figure 2. Proliferating gastric epithelium is seen in the upper right-hand corner, as well as a small quantity of necrotic débris about to be sloughed into the lumen of the stomach. The base of the ulcer shows superficial necrosis, cellular infiltration, granulation tissue, and fibrosis; the underlying omentum is fibrotic.

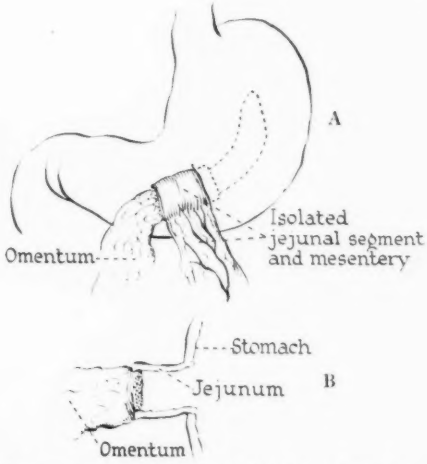

Fig. 4. Omentum implanted after it has been threaded through a cuff of jejunum. One edge of the jejunal cuff was pushed into the gastric window and fastened there so as to protect the omentum from strangulation. A, the original implant; B, a sagittal view of the result after digestion had occurred.

later after having passed bloody stools. The implanted kidney of this animal showed extensive necrosis and digestion, and the stomach and intestines were full of blood. The second dog was very ill when sacrificed 4 days after operation. A similar picture was presented of necrosis and digestion of the implant with hemorrhage into the stomach. The remaining 3 dogs, sacrificed on the 14th, 16th, and 29th days, respectively, showed partial digestion of the implant, extensive fibrosis of the exposed parenchyma, and areas of hemorrhage, infection, and necrosis (Fig. 17).

After many failures we succeeded in one dog in implanting part of the inferior lobe of the left lung in the stomach which had first been herniated through the diaphragm. The omentum, drawn up with the stomach, was tucked around the implant to prevent leakage. This animal, which remained healthy, was sacrificed on the 15th day. There had been no slipping of the structures or leakage of gastric contents. The implanted lung was found to have been digested entirely away, leaving a healing gastric stoma around a circular necrotic crater. Two other dogs, dying 2 days after operation from leakage of gastric contents and infection, showed only atelectasis and hyperemia of the implant and inflammation of its pleura.

4. Digestion of living connective tissue. In 8 dogs large round holes were made in the anterior gastric wall and the margins of the holes were sutured to the parietal peritoneum so as to expose the abdominal wall itself to the digestive action of gastric juice. After 24 hours there was hyperemia of the exposed parietal peritoneum; after 9 days the peritoneum had disappeared and there was fibrosis and digestion of the abdominal wall; after 36 days fibrosis and digestion were more marked with the production of an ulcer a few millimeters deep, the margins of which showed

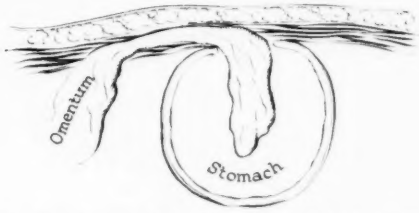

Fig. 5. A tongue of omentum implanted after passage through a tunnel in the abdominal wall. The margins of the gastric window were sewed to the parietal peritoneum so that the omentum could not be constricted by the stomach.

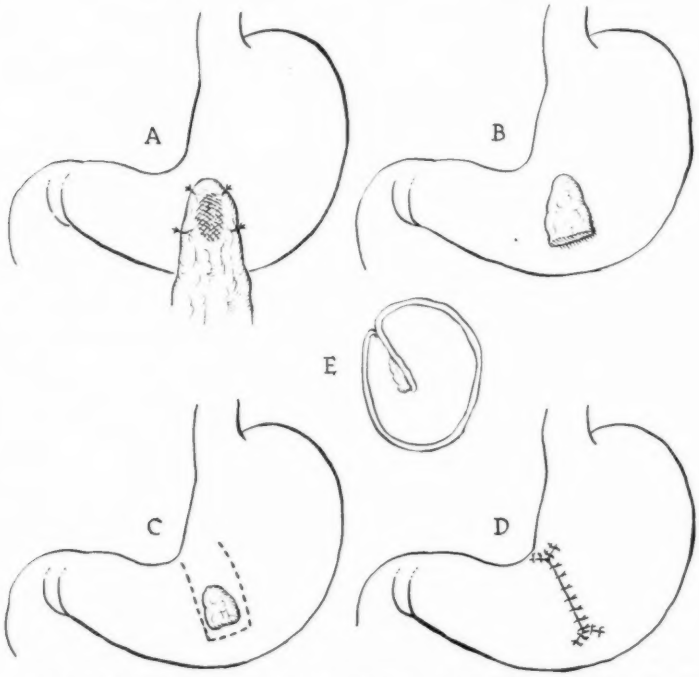

Fig. 6. Steps in the preparation and implantation of free living grafts of omentum: A, omentum fastened to the gastric wall covering a scarified area; B, parent omentum cut away after the graft had taken; C, 1 or 2 weeks later, a pedicle flap of gastric wall cut so as to include the graft; D, invagination of the flap and its parasitic graft and closure of the defect; E, sagittal view of the implant.

healing and active proliferation of gastric epithelium. One dog after 64 days had a large deep ulcer involving the fascial and muscular layers of the abdominal wall.

By a multiple-stage operation a long pedicle flap of skin was raised from the anterior abdominal wall and the free end of the flap was placed in the peritoneal cavity. A week later this flap, which appeared quite healthy, was implanted in the stomach by making a large hole in the anterior gastric wall and sewing the margins of the hole to the abdominal wall around the flap, as was done with the omentum in Figure 5. In this way we insured good circulation of skin while exposing it directly and continuously to gastric juice. One such dog sacrificed 11 days after implantation showed partial digestion of the flap, especially its subcutaneous tissue. In another dog more advanced necrosis and digestion were seen after 18 days, although the hair on the graft had grown appreciably during the period of implantation. Histologic examination of these specimens shows that epidermis is more resistant than the dermis or subcutaneous tissue to the digestive action of the gastric juice. In a third dog sacrificed after 21 days the flap had digested away entirely.

We also planted free whole thickness skin grafts, 1 to 2 centimeters in diameter, on the anterior serosal surface of the stomach and on the parietal peritoneum near the stomach. The skin took readily on these surfaces. The grafts on the stomach were implanted by turning in pedicle flaps of gastric wall (as in Fig. 6), and the grafts on the parietal peritoneum were exposed by suturing the margins of a gastric window to the abdominal wall around them (as in Fig. 5). Partial digestion of these skin grafts was noted as soon as the

Fig. 7. An isolated segment of jejunum with mesentery attached, opened along its antimesenteric border and sewed patchlike in a large gastric window. The patch is trimmed to fit the window neatly so that only jejunal mucosa is exposed to the gastric contents.

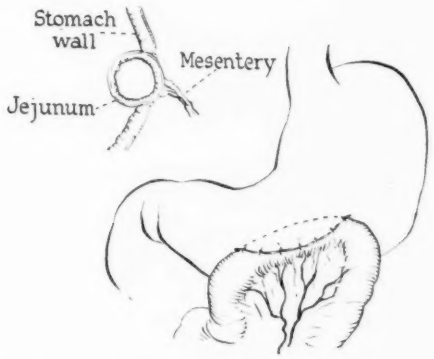

Fig. 8. Deep implantation of small intestine in the stomach. The inset shows a sagittal view of the implant.

12th day after implantation, but islands of residual epithelium could be found histologically even after 2 months.

The ends of the 10th and 11th ribs were freed and brought into the peritoneal cavity; a few days later about 3 centimeters of one or both ribs was implanted in the stomach. Complete digestion of these cartilaginous structures to the level of the gastric stoma occurred in from 12 to 17 days.

5. Digestion of living gastric tissue. Small and large areas of gastric mucosa were excised so as to expose the underlying submucous and muscular coats of the stomach to the digestive action of its own secretions. The smaller denuded areas healed rapidly. One area 1.5 by 2.5 centimeters in size was completely healed in 12 days, leaving only a minute puckered scar. On microscopic examination the muscle underlying this scar appeared perfectly normal. Larger denuded areas, 3 to 5 centimeters in diameter, required 4 to 6 weeks for healing. None of these artificial "ulcers" perforated, but histologic examination showed pronounced fibrous reaction involving the muscle layers. When, however, large portions of the stomach

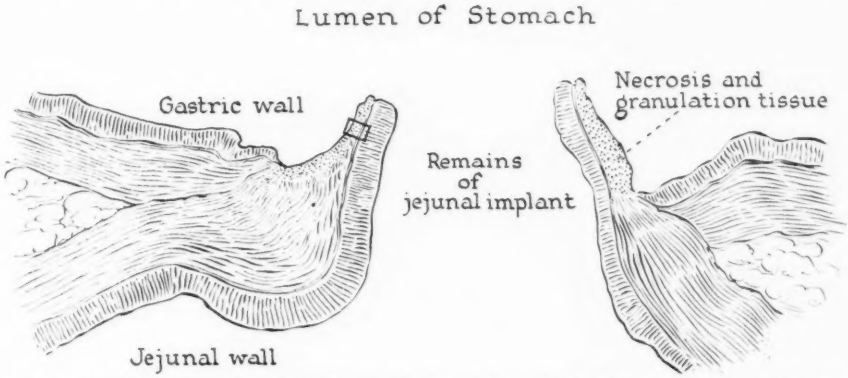

Fig. 9. Sagittal view of a deep jejunal implant after 27 days. Most of the implanted intestine had digested away leaving a large gastrojejunal fistula. The seromuscular surface of the jejunum was much more seriously affected by gastric juice than was the mucous membrane. Microscopic examination of the margins of the fistula showed no proliferative activity on the part of the jejunal mucosa, but on the other hand there was no evidence that the intestinal mucosa had been digested until its underlying wall was destroyed and its blood supply cut off. The area within the square is shown in greater detail in Figure 10.

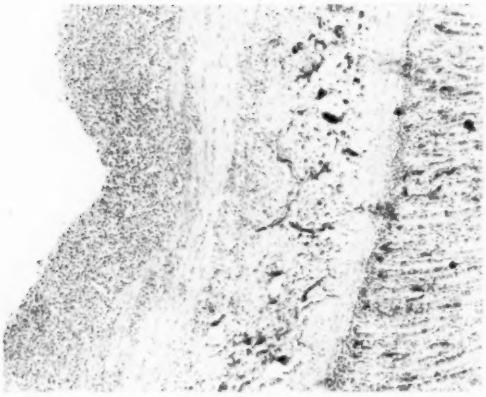

Fig. 10. Jejunal wall 27 days after implantation. Normal mucosal glands and submucosa are seen on the right, but the seromuscular layer has almost entirely disappeared. A thick layer of typical granulation tissue is seen on the left. This surface was exposed directly to the gastric contents.

Fig. 11. Section showing violent reaction of the serous surface of the colon after several days' exposure to gastric juice. The seromuscular coat is acutely inflamed with extensive necrosis. The margins of a perforation, not seen in this view, gives no evidence of proliferative activity of intestinal epithelium.

(e.g., the entire antrum and prepylorus) were deprived of mucous membrane, healing was delayed in some instances for several months. Multiple small deep ulcers were occasionally seen in these unhealed defects, and one dog died on the 49th postoperative day from perforation and peritonitis.

In 2 animals short wide flaps of gastric wall, 2.5 by 5 centimeters in size, were raised,

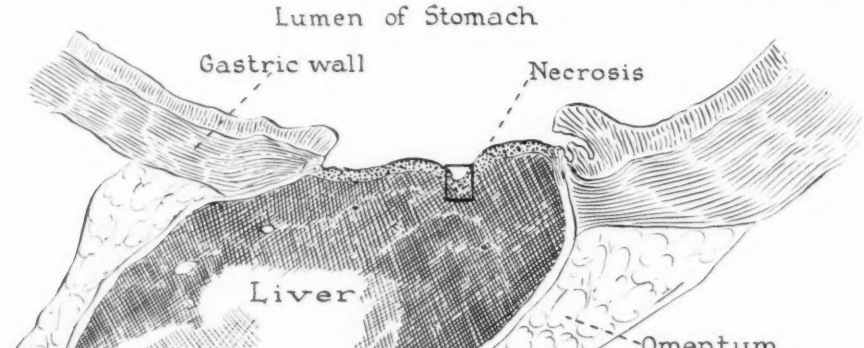

Fig. 12. Result of a deep liver implant after 26 days. The portion of the lobe, several centimeters in length, which protruded into the stomach, had digested away, leaving a shallow crater with a necrotic base. The surrounding gastric epithelium shows moderate proliferative activity.

Fig. 13. Photomicrograph of the necrotic base of the crater illustrated in Figure 12. Beneath the layer of necrosis seen in the upper right-hand corner, is a zone of fibrosis, granulation tissue, and cellular infiltration. Liver cells appear at the bottom of the picture. A small developing abscess may be observed in the lower right hand corner of the picture.

stripped of mucosa, and were then sutured back in place. In this way we attempted to expose to digestion a portion of gastric wall which lacked a protective covering of mucosa, had been subjected to a certain amount of operative trauma, and had had its circulation somewhat disturbed. These defects healed at about the same rate, however, as the denuded areas described in the preceding paragraph. There was pronounced fibrosis of the exposed muscle, but no real ulceration or perforation.

Finally, in a series of 11 dogs we turned pedicle flaps of gastric wall into the lumen of the stomach (Fig. 18). The flaps were so cut that they received an abundant blood supply from the vessels of the lesser curvature, shown by free bleeding from the tips and sides. Two of these flaps had the mucosa removed and consequently were composed of only the outer layers of the gastric wall. They were completely digested in 2 to 3 weeks. The flaps which contained mucosa showed early digestion of the serosa and muscle and delayed digestion of the mucosa; in fact, the mucous membrane had a tendency to enfold and protect its supportive structures (Fig. 18). In 2 animals in which the mucosa completely enveloped the other coats, the flap after 3 to 4 weeks had the appearance of a cone of mucosa projecting into the gastric lumen. These polypoid structures remained unchanged as long as the dogs were observed (33 and 91 days). When this protective envelopment by the mucosa failed to occur or was incomplete, the pedicle flaps disappeared in 2 to 4 weeks, leaving ulcers in the stomach wall at the site of the base of the flaps. In these animals it is

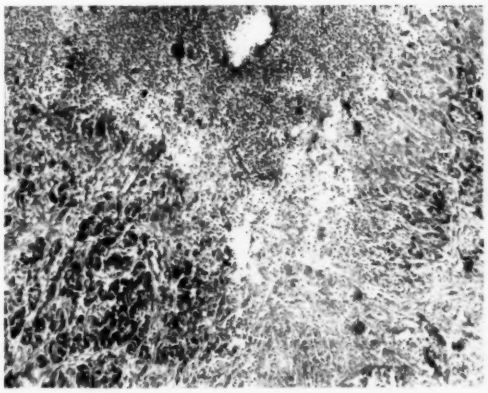

Fig. 14. Photomicrograph of a pancreatic implant after 24 days. Frank necrosis may be seen in the upper part of the field; below, islands of pancreatic cells in various stages of deterioration are separated by fibrous and granulation tissue.

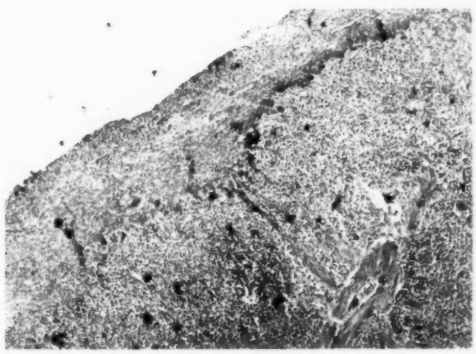

Fig. 15. Photomicrograph of an implanted spleen after 19 days. Digestion had occurred to the level of the gastric stoma. A thin zone of acute inflammatory reaction, hyalinization, and necrosis overlies the splenic parenchyma which retains its structural characteristics.

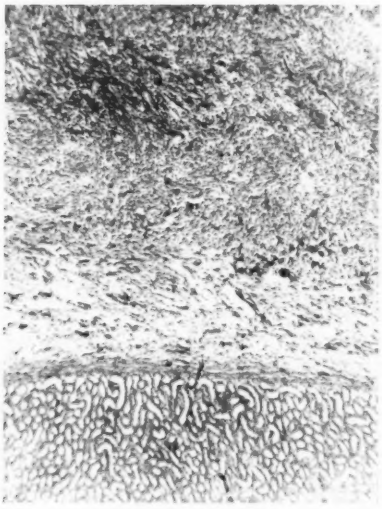

Fig. 16. Photomicrograph of a kidney 7 days after tangential implantation in a gastric window. Great thickening and fibrosis of the capsule are noted, but the parenchyma is intact and healthy.

Fig. 17. Photomicrograph which shows the digesting surface of a deeply implanted kidney. Superficially necrosis and acute inflammatory reaction are noted; more deeply can be seen hemorrhage, fibrosis, cellular infiltration, and granulation tissue, as well as a degenerating glomerulus and the remains of collecting tubules.

probable that the seromuscular layers of the flaps were destroyed and that the mucosa, deprived of support and circulation, thereupon underwent digestion also.

OBSERVATIONS

It may be questioned whether additional factors such as strangulation, infarction, infection or autolysis may not have contributed to the results which we have called gastric digestion. The question of constriction actually arises only in the case of solid tissues or organs where more or less unyielding structures are implanted through a gastric window which in time undergoes contraction. In those preparations care was taken to avoid constriction at the time of implantation, and subsequent microscopic examination of the implanted tissues shows the vessels in most instances to be normally filled with blood. Moreover, abnormal cellular changes are found as a rule only at or near the corroding surface and not in the body of the implant as would be expected if the circulation of the entire implant were compromised. Since our implants were all made in the normal fasting acid stomach, a high percentage of infections would not be expected and in fact were not found. Leucocytic infiltration and abscesses were observed in some of the implants, but that was exceptional. Histologic examination also appears to rule out autolysis as a primary factor in the so called digestion since there was no generalized deterioration of cells throughout the implant. The evidence seems fairly conclusive, therefore, that living tissue of all sorts may actually be digested in the stomach, either directly or after necrosis has occurred, in the absence of contributing factors such as strangulation, infection and autolysis.

Living tissues vary in susceptibility to gastric digestion. Judged by the time required for digestion when placed in the stomach tissues may be arranged tentatively in order of resistance of digestion. Most susceptible are the seromuscular coats of the intestine and gall bladder; next, omentum and cartilage; then kidney, spleen, lung, liver, and pancreas; and most resistant of all, fibrous connective tissue, skin, and intestinal mucosa.

The only tissue which appears to be completely immune to ordinary gastric digestion

is the epithelium of the stomach. Thin sheets of regenerating gastric epithelium, even those which seem to be poorly supported and nourished by underlying structures, show no signs of injury from gastric juice. The reason for this immunity is not clear. It has been suggested that the presence of a protective coat of mucin prevents digestion, but Dragstedt and his associates state that the most advanced cells in the proliferative process may be entirely devoid of mucin. It is noteworthy that tissues, once covered by regenerating gastric epithelium, are protected from digestion. This is an important feature of the process of repair in the stomach.

An impression gained from this study is that fibrosis, a reaction most strikingly seen in the omentum, hinders digestion and therefore acts as a protective mechanism for more highly differentiated tissue. Granulation tissue seems to provide an even more resistant surface. It is important to note in this connection that certain tissues respond to the presence of acid pepsin with considerable fibrous reaction and round cell infiltration, whereas others undergo disintegration and digestion at the surface without much reaction.

Tissues also vary in the type of reaction to gastric juice. Serous surfaces in general become acutely inflamed with leucocytic infiltration and necrosis, as in Figure 11. The omentum and the capsules of liver, spleen and kidney usually respond with excessive amounts of fibrosis, as in Figures 3 and 16. The parenchyma of solid viscera characteristically present complex pictures of fibrosis, hemorrhages, cellular infiltration, and necrosis (Figs. 13, 14, 15, and 17). Some tissues, muscle for example, tend to produce granulation tissue at the corroding surface, as in Figure 10. Epidermal surfaces seem to erode slowly with little or no cellular reaction.

Organs and tissues which project into the lumen of the stomach are much more rapidly and completely digested than are those placed tangentially in a gastric window. An attractive conjecture is that deep implants, lacking adequate protective coats of mucin, are subject to digestion, whereas tangential implants and residual craters of digested implants are protected from the full corrosive effects of acid pepsin by mucin from the surrounding gastric mucosa.

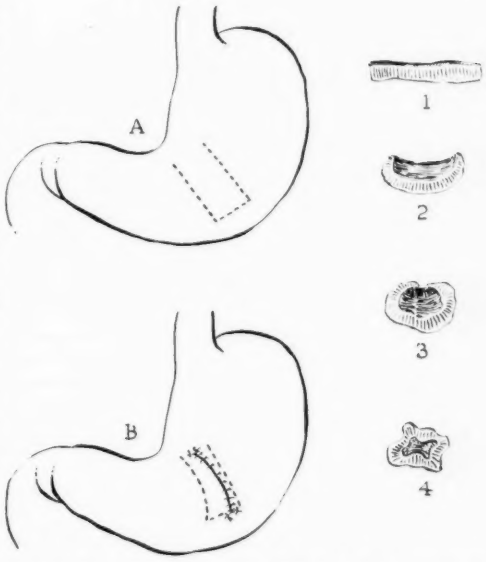

Fig. 18. Method of turning in a pedicle flap so as to expose the structures of the gastric wall to the digestive action of its own secretions. The small figures illustrate the tendency of such flaps to curl, the more resistant mucosa enveloping the less resistant seromuscular layer.

It should be noted finally that a number of our animals appeared toxic, some were quite ill in fact, during the period of necrosis and digestion of the implants; but these animals recovered full health after the necrotic tissue had disappeared. This phenomenon was observed particularly after implantation of intestines, gall bladder, and solid organs.

SUMMARY AND CONCLUSIONS

An experimental study has been made to determine whether or not living tissues are susceptible to ordinary gastric digestion. Many different tissues, including omentum, intestine, liver, gall bladder, pancreas, spleen, kidney, lung, cartilage, skin, and even the gastric wall itself, were subjected to gastric digestion in healthy dogs. The test was made by means of implanting living tissues and organs in the lumen of the stomach or by insuring prolonged surface contact with gastric secretion.

Virtually all the tissues and organs so tested underwent digestion. There is evidence that this digestion occurred, in many instances at least, in the absence of contributing factors of strangulation of the implant, infarction, infection, or autolysis.

The tissues most rapidly digested were the external coats of hollow organs (intestines, appendix, gall bladder); those most resistant were fibrous connective tissue, skin, and intestinal mucosa. The seromuscular coat of the stomach itself was not exempt from autodigestion. The one tissue which seemed to be immune to ordinary digestion was gastric epithelium.

Organs and tissues projecting into the lumen of the stomach were much more rapidly and completely digested than were those which were placed tangentially in a gastric window.

Living tissues undergoing digestion showed different sorts and degrees of reaction. Serous surfaces in general became acutely inflamed with rapid leucocytic infiltration and necrosis. The omentum and the capsules of liver, spleen, and kidney responded with excessive amounts of fibrosis. The parenchyma of solid viscera characteristically presented complex pictures of fibrosis, hemorrhages, cellular infiltration, and necrosis. Some tissues, muscle for example, tended to produce granulation tissue at the corroding surface. Epidermal surfaces slowly eroded with little or no cellular reaction.

Histologic study suggests that a surface of active fibrosis offers a certain amount of resistance to digestion, that even more opposition is offered by a layer of granulation tissue, and that these surfaces act as barriers to the destructive action of acid chyme. Such tissue responses are probably of practical importance since they serve as protective mechanisms, delaying the progress of corrosion until healing can take place by means of fibrous contraction of the gastric defect and proliferation of gastric epithelium across the base of the ulcer. Once tissues are covered with proliferating gastric epithelium, they appear to be safe from further corrosive action of normal gastric juice.

A number of the dogs appeared toxic during the period of necrosis and digestion of the implants, but recovered full health after the necrotic tissue had disappeared.

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THE LOCAL APPLICATION OF NITROFURAN COMPOUNDS WITH SPECIAL REFERENCE TO USE ON WOUNDS

M. C. DODD, Ph.D., F. W. HARTMANN, Sc.D., and W. C. WARD, M.S.

IN a previous report (4) a series of nitrofuran compounds was shown to be bacteriostatic and bactericidal for a variety of gram positive and gram negative organisms in low concentrations. Further work has established the fact that the bactericidal activity of several of these compounds is not abolished by the presence of blood or serum.

Previous work has also shown that some of these compounds are nontoxic for laboratory animals in moderately large doses.

These facts suggested the possible clinical use of nitrofuran compounds in the treatment of infected wounds. In order to test the value of this suggestion as far as possible in the laboratory and to provide maximum information to the clinician, an examination was made of the irritant properties, toxicity, and effect on the healing rate of wounds in rabbits produced by the local application of nitrofuran compounds. For this purpose, five of these compounds previously shown to have excellent antibacterial properties *in vitro* were selected. The 5 compounds chosen were—

	R = O_2N–	Solubility in water
5-nitro-2-furyl methyl ketone	–R–$COCH_3$	1–250
5-nitro-2-furaldehyde semicarbazone	–R–CH=N–$NHCONH_2$	1–5000
n-propyl-5-nitro-2-furoate	–R–$COOC_3H_7$	1–10,000
5-nitro-2-furfuryl propionate	–R–$CH_2OOCC_2H_5$	1–1000
ethyl β–(5-nitro-2-furyl) acrylate	–R–CH=$CHCOOC_2H_5$	1–15,000

The first four may be regarded as derivatives, in the order named, of furan, 2-furaldehyde, 2-furoic acid and 2-furfuryl alcohol, while the last named compound is related to β–(2-furyl) acrylic acid.

The relatively low solubility of four of these compounds in water has already been indicated. For the following experiments they were incorporated into a water soluble base composed of polyethylene glycols (carbowaxes) and propylene glycol.[1] The semicarbazone and the furoate formed pharmaceutically acceptable preparations in this base while the other three compounds caused a progressive discoloration of the base. However, *in vitro* tests on the discolored products showed no loss of antibacterial activity even after storage for 1 year.

In these experiments this base was found to be quite suitable as a vehicle for the application of these antibacterial compounds. All of the nitrofuran compounds are soluble in the base thus providing a vehicle by which greater concentrations of the compounds could be applied than would be otherwise possible unless the compounds were placed directly on the wounds. In avoiding this latter procedure, a more economical preparation was obtained even though the concentrations used in the base are many times the minimum bactericidal concentrations of the compounds. Keeping in mind that the primary clinical use for these compounds would be in the treatment of infected wounds, a preparation of this kind also avoids the caking and interference with wound drainage so frequently encountered with powdered preparations and heavy ointments. In addition, the slight surface active properties of carbowaxes, plus the fluidity of the preparation at body temperature should provide a mechanism for a maximum of spreading and mixing of the compounds with body fluids even when pus or other organic material is present. Finally, the preparation being washable can be removed readily with water and facilitates observation and redressing of wounds.

The base alone was used as a control in the experiments on the healing rate of treated wounds. It is nonfatty, contains no water, and possesses physical characteristics suitable for use as a vehicle for local application. Extensive work by Smyth and coworkers (13, 14) has demonstrated the lack of toxicity and irritation of the carbowaxes for laboratory animals and that they produced no more irritation in human subjects than such commonly used bases as petrolatum and glycerin. Friedman has shown that carbowax 1500 is also nontoxic for rabbits when given intravenously in large doses. Numerous investigations (1, 6, 7, 10, 16) have been reported on the safety of propylene glycol for human use.

[1] Carbowax 1500—55%
Carbowax 4000—20%
Propylene glycol—25%

TABLE I.—IRRITATION TESTS ON HUMAN SUBJECTS WITH FIVE NITROFURAN COMPOUNDS—RESULTS OF EXAMINATION AFTER 6, 24, AND 48 HOURS

Subject	5-nitro-2-furyl methyl ketone 1–500			5-nitro-2-furaldehyde semicarbazone 1–500			n-propyl-5-nitro-2-furoate 1–500			5-nitro-2-furfuryl propionate 1–100			ethyl β–(5-nitro-2-furyl) acrylate 1–500		
Number	6	24	48	6	24	48	6	24	48	6	24	48	6	24	48
1	–*	–	±	–	–	–	–	–	–	–	–	–	–	–	+
2	–	–	+**	–	–	–	–	–	–	–	–	–	–	–	+
3	–	–	–	–	–	–	–	–	–	–	–	–	–	–	+
4	–	–	+	–	–	–	–	–	–	–	–	–	–	+	+
5	–	–	–	–	–	–	–	–	–	–	–	–	–	–	+
6	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
7	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
8	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	+
10	–			–			–			–			–		
Total Reactions	0	0	3	0	0	0	0	0	0	0	0	0	0	1	6

*(–) = no skin reaction.
**(+) = hyperemia of skin.

IRRITATION TESTS ON HUMAN SKIN

The five aforementioned nitrofuran compounds were tested for possible irritation effect on human skin. Four compounds, the ketone, semicarbazone, furoate and furylacrylate were used at a concentration of 1:500 in the base, while the propionate was tested at a concentration 1:100 in the same preparation. All five preparations were applied to the forearms of each of 10 volunteers for 2 successive days. Following application, the areas used were covered by small dressings. Sufficient material was applied to insure its presence on the skin for 24 hours. Observations of all areas were made at 6, 24, and 48 hours following application.

Table I shows that none of the five nitrofuran compounds was irritating after 6 hours contact. After 24 hours one subject showed hyperemia of the skin due to the presence of the furylacrylate. After 48 hours, 6 individuals out of 9 gave evidence of irritation due to this same compound, while 3 out of 9 persons were affected by the ketone. None of the reactions were more severe than a moderate hyperemia. Apparently, these two compounds possess irritating properties for two-thirds and one-third, respectively, of the individuals tested at the concentrations used in the experiment. The other three compounds gave no evidence of irritation in any of the subjects in the concentrations tested.

EFFECT OF FIVE NITROFURAN COMPOUNDS ON THE HEALING RATE OF EXPERIMENTAL WOUNDS IN RABBITS

For this experiment the 5 nitrofuran compounds here mentioned were incorporated into the washable base in three different concentrations. The ketone, furylacrylate, semicarbazone and furoate were made up in concentrations of 1:500, 1:1000, and 1:5000 in the base, while the propionate was compounded at 1:100, 1:500, and 1:1000. These concentrations were selected rather arbitrarily, al-

TABLE II.—HEALING TIME IN DAYS OF WOUNDS TREATED WITH 5-NITRO-2-FURYL-METHYL KETONE

Concentration	Average healing time for wounds on ventral surface	Average healing time for wounds on dorsal surface	Average healing time for all wounds	Shortest healing time for any wound	Longest healing time for any wound
1:500	21	17	19	12	28
1:1000	20	16	18	12	26
1:5000	17	17	17	10	22
Base	15	17	16	10	20
Untreated	14	14	14	10	16

though all of them are many times the minimum bactericidal concentration for these compounds as determined by *in vitro* methods. The fact that the previous experiment had shown the 1:500 concentrations of the ketone and furylacrylate to be irritating suggested that these concentrations would also interfere with the healing process, thus providing some information on the maximum concentration permissible for wound treatment. The following data, however, do not support this expectation since these concentrations show very little effect on the healing process, though they may not be optimal for use on healing wounds.

Twenty rabbits were used in the experiment and 5 to 8 wounds were inflicted on each rabbit. After removal of the hair from either the dorsal or ventral surface of the rabbits, the wounds were made with a rongeur and scalpel. The technique employed produced wounds quite similar in size and of equal depth. The wounds averaged 175 square millimeters in area and extended down to the muscle. The wounds on the ventral surface were observed to stretch more and become larger than those on the dorsal surface, which was attributed to the thinness and lack of connective tissue in the former as compared to the skin on the back.

The three concentrations of each compound in the base were applied to these wounds, and the effect on the healing rate was compared with untreated wounds and wounds treated with the base alone. The test substances were reapplied every 2 days, and sufficient material was applied to cover the wounds completely. The wounds were protected by small gauze and adhesive bandages ("Band Aid") and removal was prevented by cloth jackets tied around the rabbits. Their progress in healing was followed by the method of Carrel and Hartmann. Before each treatment tracings of the wounds were made on cellophane. These were transferred to plain white paper for measurement with a compensating polar planimeter. The process of healing was thus measured and recorded until complete healing occurred, which for these experiments was defined as the time when the new epithelium over the wound became continuous.

Fourteen days after the wounds were made biopsies obtained from those treated with each of the concentrations of the five compounds as well as from the control wounds were subjected to histological examination for evidence of possible irritation or injury due to nitrofuran compounds and as a further comparison of healing rates.

The results of this experiment can best be considered by presentation of the data obtained on each compound in order. A total of 130 wounds were observed, each compound being used on 18 wounds, 6 on each of the 3 concentrations employed. The tables and graphs which follow are based on the data obtained from 3 to 6 rabbits. Two control wounds were used on each animal, one untreated and one to which the base alone was applied.

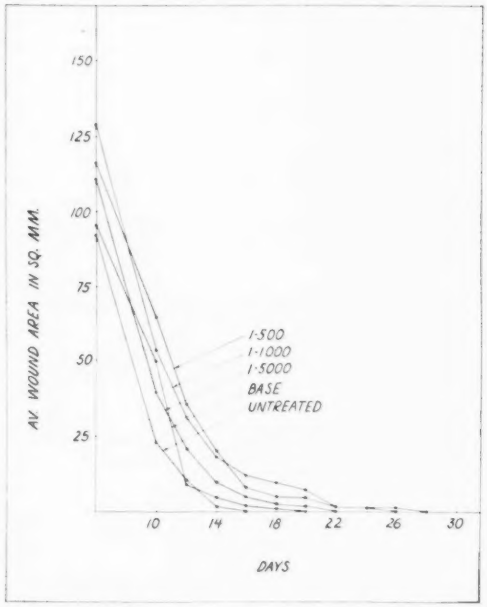

Fig. 1. Healing rates of wounds treated with 5-nitro-2-furyl methyl ketone, 1:500, 1:1000, and 1:5000 in a washable base. The inhibitory action of the three concentrations of the compound on epithelization is apparent after the 16th day.

The effect of 5-nitro-2-furyl methyl ketone on the healing rate of wounds in rabbits is demonstrated in Table II and Figure 1. A comparison of columns 2 and 3 in Table II shows that the variation in healing time between wounds on the dorsal and ventral surfaces of the animals was not significant. Column 4 demonstrates that the average healing rate was inhibited by this compound, the degree of inhibition increasing with the concentration. Columns 5 and 6 show that the process of wound repair progressed at a very different rate from animal to animal, emphasizing both the individual differences between animals and the value of controls on each.

Since the decrease in the area of the wounds between successive measurements varied directly with the rate of healing, the average areas of the

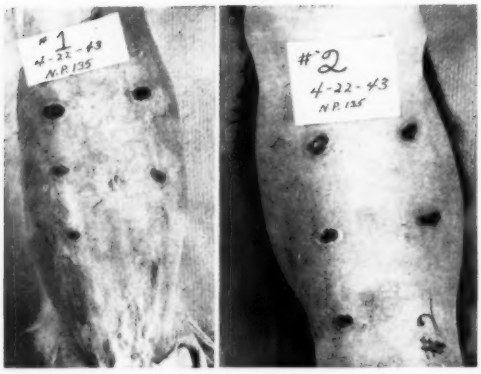

Fig. 2, left. Rabbit 1 on the 10th day of treatment with 5-nitro-2-furyl methyl ketone (N.P. No. 135). Wounds. Upper left, 1:500. Upper right, 1:1000. Middle left, 1:5000. Middle right, base alone. Lower left, untreated.

Fig. 3. Rabbit 2 on the 10th day of treatment with 5-nitro-2-furyl methyl ketone (N.P. No. 135). Wounds. Upper left, 1:500. Upper right, 1:1000. Middle left, 1:5000. Middle right, base alone. Lower left, untreated.

wounds were plotted against time for a graphic presentation of the effect of the various concentrations of the ketone on the healing rate. Experience had shown any significant variation in the process of wound repair to occur in the second half of the total healing period, hence the initial wound areas presented in all the graphs included here are those obtained on the sixth day of treatment.

Figure 1 shows the marked similarity in the rate of healing of all wounds used in the study of 5-nitro-2-furyl methyl ketone, but also demonstrates the inhibitory effect produced by this compound on the rate at which final epithelization of the treated wounds occurred. The initial sizes of the wounds were similar, and the healing rate curves all have essentially the same slope until about the sixteenth day. From this point on, during the time when the process of epithelization was observed to be the major repair process, the inhibition of healing produced by the compound is apparent. It should be recalled that this compound was irritant to intact human skin at a concentration of 1:500.

The gross appearance of the wounds treated with 5-nitro-2-furyl methyl ketone and with the base alone was essentially the same as the untreated wounds (Figs. 2, 3) except that the latter did not develop as heavy a crust as the treated wounds.

Table III presents the observations made on the healing time of wounds treated with ethyl β-(5-nitro-2-furyl) acrylate. In this group of animals the wounds on the dorsal surface healed more rapidly than did those on the ventral surface. Columns 5 and 6 again emphasize the individual differences in animals, showing that the slowest healing wounds required more than twice as much time as the fastest. The data in column 4 indicate that the test compound had no appreciable effect on healing when present at a concentration of 1:5000, but did produce a slight extension of healing time at 1:1000 and 1:500.

Figure 4 graphically demonstrates the inhibitory effect of the higher concentrations of ethyl-β-(5-nitro-2-furyl) acrylate on the healing of wounds as compared to controls treated with the base alone and to untreated controls. This effect appears to be similar to that produced by the previously described compound in that it occurs late in the process of healing, at the time of final epithelization, although the effect in this instance is not as marked. Grossly all wounds appeared similar (Figs. 5 and 6).

The data in column 4, Table IV, show that the third test compound, 5-nitro-2-furfuryl propionate definitely slowed the healing process in all three concentrations employed, although this effect was no more marked at 1:100 than it was at a 1:1000 concentration. Columns 2 and 3 again show that wounds on the back healed a little sooner, and columns 5 and 6 emphasize the previous data pointing to the wide variability in the healing rate of wounds on individual animals.

TABLE III.—HEALING TIME IN DAYS OF WOUNDS TREATED WITH ETHYL β(5-NITRO-2-FURYL) ACRYLATE

Concentration	Average healing time for wounds on ventral surface	Average healing time for wounds on dorsal surface	Average healing time for all wounds	Shortest healing time for any wound	Longest healing time for any wound
1:500	19	16	17.5	12	26
1:1000	20	13	16.5	10	28
1:5000	16	14	15	10	24
Base	16	14	15	10	22
Untreated	15	13	14	10	22

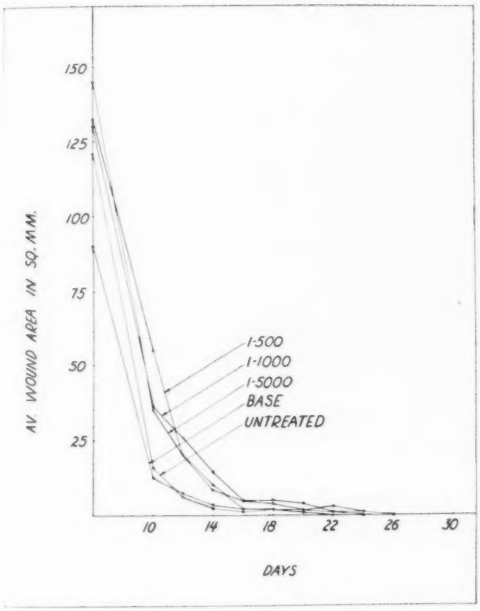

Fig. 4. Healing rates of wounds treated with ethyl β—(5-nitro-2-furyl) acrylate, 1:500, 1:1000, and 1:5000 in a washable base. The higher concentrations prolong the healing time of wounds as compared to the control wounds. This effect is most apparent in the period after the sixteenth day.

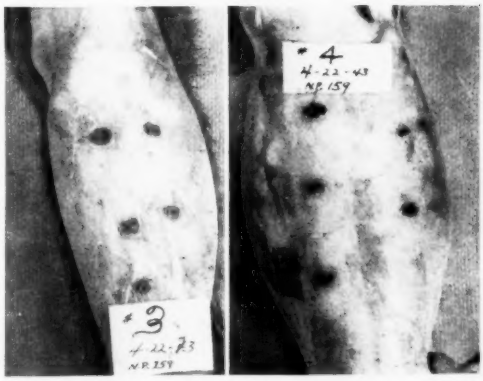

Fig. 5, left. Rabbit No. 3 on the 10th day of treatment with ethyl β—(5-nitro-2-furyl) acrylate (N.P. No. 150). Upper left, 1:500. Upper right, 1:1000. Middle left, 1:5000. Middle right, base alone. Lower left, untreated.

Fig. 6. Rabbit No. 4 on 10th day of treatment with ethyl β—(5-nitro-2-furyl) acrylate (N.P. No. 150). Wounds. Upper left, 1:500. Upper right, 1:1000. Middle left, 1:5000. Middle right, base alone. Lower left, untreated.

Figure 7 illustrates the slight prolongation of healing time produced by all three concentrations of this compound as compared to the control wounds. The gross appearance of the treated wounds as shown in Figures 8 and 9 was not significantly different from those receiving no treatment.

The results of the treatment of wounds with n-propyl-5-nitro-2-furoate are presented in Table V. The figures in column 4 indicate that this compound had no significant effect on the healing process as noted with the previous compounds. The apparently anomalous result of 17.5 days average for the healing of wounds treated with a concentration of 1:1000 must be discounted as perhaps due to some unrecognized error, since wounds treated with both the larger and smaller concentrations healed, on the average, in a period of time equal to that of the untreated controls and somewhat sooner than that of those treated with the base alone. The previously noted tendency of wounds on the back to heal more quickly than on the ventral surface is again apparent in this group of animals as listed in columns 2 and 3. Again, the variability in the healing of wounds on individual animals is emphasized by the shortest and longest healing time observed for any wound given in columns 5 and 6.

Figure 10 illustrates the similarity of all wounds in this group both treated and untreated, empha-

TABLE IV.—HEALING TIME IN DAYS OF WOUNDS TREATED WITH 5-NITRO-2-FURFURYL PROPIONATE

Concentration	Average healing time for wounds on ventral surface	Average healing time for wounds on dorsal surface	Average healing time for all wounds	Shortest healing time for any wound	Longest healing time for any wound
1:100	18	16	17	12	24
1:500	17	16	16.5	10	24
1:1000	18	16	17	12	24
Base	15	13	14	10	20
Untreated	14	12	13	12	16

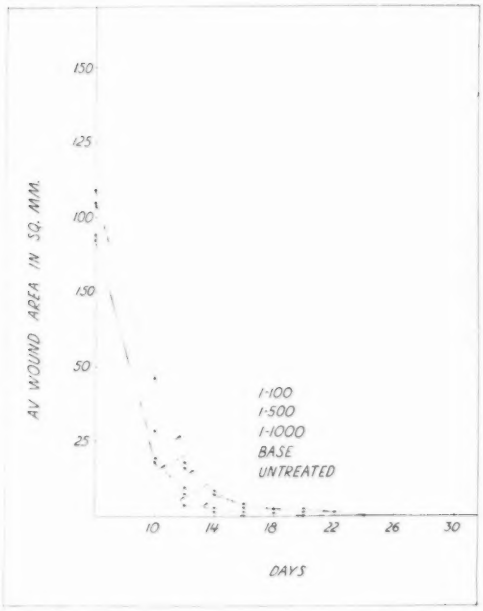

Fig. 7. Healing rates of wounds treated with 5-nitro-2 furfuryl propionate, 1:100, 1:500 and 1:1000 in a washable base. All three concentrations slowed the rate of treated wounds as compared to wounds treated with the base alone or untreated wounds.

Fig. 8, left. Rabbit No. 5 on the 10th day of treatment with 5-nitro-2-furfuryl propionate (N.P. No. 225), 1:100, 1:500 and 1:1000 in a washable base. Wounds. Upper left, 1:100. Upper right, 1:500. Middle left, 1:1000. Middle right, base alone. Lower left, untreated.

Fig. 9. Rabbit No. 6 on the 10th day of treatment with 5-nitro-2-furfuryl propionate (N.P. No. 225), 1:100, 1:500, and 1:1000 in a washable base. Wounds. Upper left, 1:100. Upper right, 1:500. Middle left, 1:1000. Middle right, base alone. Lower left, untreated.

sizing the lack of any inhibitory action due to the presence of this compound (see also Figs. 11 and 12). Even the previously noted and unexplained results obtained with wounds treated with a concentration of 1:1000, do not produce a markedly dissimilar healing rate or modify the gross appearance of all the wounds in this group.

The results in Table VI are from wounds treated with 5-nitro-2-furaldehyde semicarbazone. Column 4 shows that this compound is like the previous one in that none of the three concentrations tested had any inhibitory effect on the rate of healing as compared to either wounds treated with the base alone or untreated wounds. In fact, wounds treated with a concentration of 1:1000 of this compound showed an average healing time shorter than the controls. Figure 13 emphasizes the similarity of the healing process of all wounds in this group of animals, and Figures 14 and 15 show the wounds on two of these rabbits on the tenth day of treatment.

In summary, it can be noted that three of the nitrofuran compounds tested, 5-nitro-2-furyl methyl ketone, ethyl β-(5-nitro-2-furyl) acrylate and 5-nitro-2-furfuryl propionate caused a slight prolongation of the healing time of wounds in rabbits, while no such effect was observed in wounds treated with either n-propyl-5-nitro-2-furoate or 5-nitro-2-furaldehyde semicarbazone. No other effect was noted with any of the compounds. A review of the tabulated general average healing periods for wounds treated with the

TABLE V.—HEALING TIME IN DAYS OF WOUNDS TREATED WITH N-PROPYL-5-NITRO-2-FUROATE

Concentration	Average healing time for wounds on ventral surface	Average healing time for wounds on dorsal surface	Average healing time for all wounds	Shortest healing time for any wound	Longest healing time for any wound
1:500	10	14	15	12	20
1:1000	19	16	17.5	10	26
1:5000	14	16	15	10	20
Base	18	16	17	12	22
Untreated	10	11	15	10	22

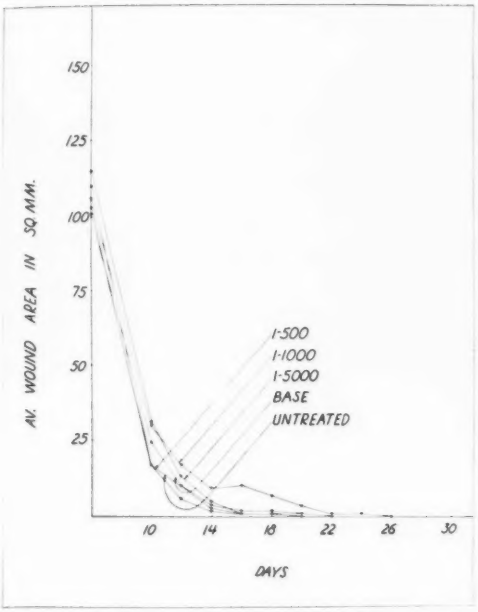

Fig. 10. Healing rates of wounds treated with n-propyl-5-nitro-2-furoate, 1:500, 1:1000 and 1:5000 in a washable base. This compound did not significantly affect the healing time of treated wounds as compared with the controls.

Fig. 11, left. Rabbit No. 7 on the 10th day of treatment with n-propyl-5-nitro-2-furoate, (N.P. No. 245), 1:500, 1:1000, and 1:5000 in a washable base. Wounds. Upper left, 1:500. Upper right, 1:1000. Middle left, 1:5000. Middle right, base alone. Lower left, untreated.

Fig. 12. Rabbit No. 8 on the 10th day of treatment with n-propyl-5-nitro-2-furoate, (N.P. No. 245), 1:500, 1:1000, and 1:5000 in a washable base. Wounds. Upper left, 1:500. Upper right, 1:1000. Middle left, 1:5000. Middle right, base alone. Lower left, untreated.

three inhibitory compounds shows the greatest increase in healing time, as compared to that for the wounds on which the base alone was used, was 3 days. This delay in healing is not marked in comparison with that found by other investigators using some commonly employed therapeutic substances on experimental wounds. For example, Brush and Lam found that crystalline urea delayed healing of wounds in guinea pigs 8 to 18 days longer than that for controls, while Skinner and Waud found that tannic acid (5 per cent aqueous) and strong triple dye (brilliant green 2.5 per cent, neutral acriflavine 2.5 per cent, and gentian violet in water) extended healing time of burns in rabbits, 5 and 40 days respectively.

A histological examination of tissue taken from both treated and untreated wounds on animals in all test groups on the fourteenth day of treatment was done. The results corroborated the above observations that the only effect produced by the compounds was a slight inhibition of healing by the three named above. This examination failed to emphasize even this effect since little or no difference could be found between treated and untreated tissue regardless of the compound used.

TOXICITY OF NITROFURAN COMPOUNDS BY ABSORPTION FROM LARGE WOUNDS

The following experiment was designed to determine possible toxicity of the nitrofuran com-

TABLE VI.—HEALING TIME IN DAYS OF WOUNDS TREATED WITH 5-NITRO-2-FURALDEHYDE SEMICARBAZONE

Concentration	Average healing time for wounds on ventral surface	Average healing time for wounds on dorsal surface	Average healing time for all wounds	Shortest healing time for any wound	Longest healing time for any wound
1:500	16	12	14	10	20
1:1000	10	13	11.5	10	14
1:5000	14	12	13	10	16
Base	14	13	13.5	10	16
Untreated	15	13	14	12	16

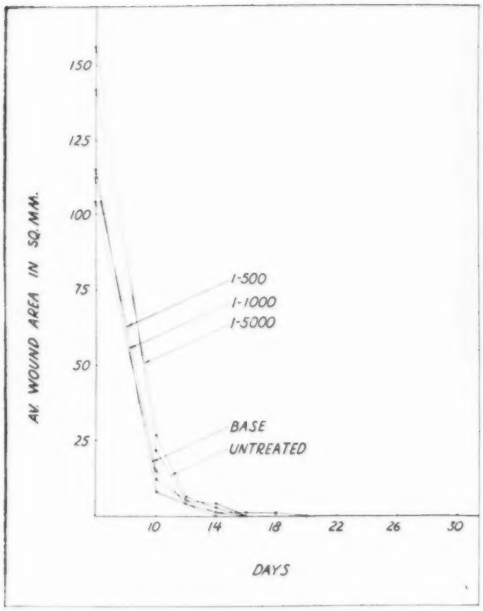

Fig. 13. Healing rates of wounds treated with 5-nitro-2-furaldehyde semicarbazone, 1:500, 1:1000, and 1:5000 in a washable base. No inhibitory effect on the healing rate was observed in wounds on which this compound was employed. The wounds treated with a 1:1000 concentration healed even faster than the controls.

pounds discussed in the work described by continuous absorption from large wounds when the compounds were present over a prolonged period. The conditions are thus similar to the clinical use of local antiseptics on large wounds. Toxicity under such conditions depends on, first, absorption of the compound, and second, its toxic properties.

An idea of this second factor for each of the five compounds tested can be gained from the data to be given on the L.D. 50 for mice and rats by the oral and subcutaneous routes of administration. It must be borne in mind, however, that these figures cannot be applied directly to rabbits on which the present work was done, but merely

Compound	L.D. 50—Mice orally mgm./kgm.	L.D. 50—Rats subcutaneously mgm./kgm
5-nitro-2-furyl methyl ketone	400	200
5-nitro-2-furaldehyde semicarbazone	600–700	>3000
n-propyl-5-nitro-2-furoate	1200	>2000
5-nitro-2-furfuryl propionate	300	700
ethyl β—(5-nitro-2-furyl) acrylate	3500	>4000

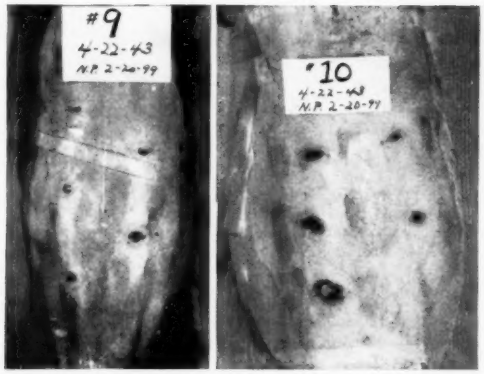

Fig. 14, left. Rabbit No. 9 on the 10th day of treatment with 5-nitro-2-furaldehyde semicarbazone, (N.P. No. 2–20–99), 1:500, 1:1000, and 1:5000 in a washable base. Upper left, 1:500. Upper right, 1:1000. Middle left, 1:5000. Middle right, base alone. Lower left, untreated.

Fig. 15. Rabbit No. 10 on the 10th day of treatment with 5-nitro-2-furaldehyde semicarbazone, (N.P. No. 2–20–99), 1:500, 1:1000, and 1:5000 in a washable base. Upper left, 1:500. Upper right, 1:1000. Middle left, 1:5000. Middle right, base alone. Lower left, untreated.

serve to indicate the toxicity found under controlled methods of administration.

Because of the lack of a chemical test to determine the presence of the compounds in the blood, the dosage applied to the wounds in this experiment was large, with the hope that toxic symptoms might be produced which could be detected by either gross or microscopic methods, thus indicating the occurrence or lack of absorption. Accordingly, the animals were exposed to approximately 250 milligrams per kilogram of each compound continuously for a month as indicated. This dosage is obviously much lower in many cases than that given, but the fact of the continuous presence of the compounds made the conditions rather severe.

The method of application consisted of the preparation of large wounds with areas of approximately 25 to 50 square centimeters on the ventral surface of the rabbits to which the compounds were continuously applied for a period of 4 weeks. The appropriate dose of the substance was concentrated in approximately 2 grams of the washable base previously described and applied to a square piece of gauze which was placed over the wounds and held in place with adhesive tape. A cloth jacket was then tied in place over all to protect the dressings. The compounds were applied immediately after the wounds were made and at weekly intervals afterward. This ensured an excess of material in contact with the wounds

at all times. Weight records, blood examinations and blood urea nitrogen determinations were done before and after the treatment period. Urine analyses were useless because of the tendency of many apparently normal rabbits to albuminuria. At the termination of the experiment, all animals were sacrificed and the tissues were studied microscopically.

5-Nitro-2-furyl methyl ketone was the only one of the five compounds tested to produce death or symptoms of toxemia. The 2 rabbits treated with this compound as outlined died in 24 to 48 hours. Four more rabbits treated by the same method but with a dosage of 100 to 200 milligrams per kilogram also died in 1 to 2 days. However, 50 and 65 milligrams per kilogram were applied, as has been described, for a full month without any symptoms of toxemia, nor did the histological examination reveal any abnormalities present in any of the tissues.

The other four compounds were used at the stated dose on two rabbits each for the full experimental period of 4 weeks without any symptoms of toxemia appearing. None of the rabbits showed a significant weight variation. The blood picture was essentially normal, the only possible significant finding being a slightly lower hemoglobin value. Blood urea nitrogen determinations were well within the limits determined on normal rabbits. The histological examination of the tissues of these animals was also entirely negative for any abnormalities attributable to the compounds.

Observations were made on the wounds during this period although because of the large concentration of compounds present no attempt was made to measure the effect on healing. However, no gross sign of irritation was observed. Heavy crusts or scabs formed over all wounds regardless of the compound applied. However, differences were observed. Ethyl β—(5-nitro-2-furyl) acrylate, n-propyl-5-nitro furoate and 5-nitro-2-furaldehydes emicarbazone caused a considerable quantity of tough, elastic necrotic tissue to be formed in wounds on which these compounds were present. Less of this material was noted in wounds treated with 5-nitro-2-furyl methyl ketone and none was found when 5-nitro-2-furfuryl propionate was used.

As a result of this experiment it can be concluded that four of the five compounds discussed here are nontoxic for rabbits when applied to large open wounds in doses of approximately 250 milligrams per kilogram of body weight continuously for 4 weeks. One compound, 5-nitro-2-furyl methyl ketone, is toxic under similar conditions, causing the death of rabbits in 1 to 2 days. However, no toxicity was encountered when the quantity of chemical applied was reduced to 50 to 65 milligrams per kilogram.

COMMENT

Previous work has established the antibacterial action of the five nitrofuran compounds discussed here, which suggested an investigation of their possible use in the local treatment of infected wounds. Compounds intended for such a purpose should also be nonirritating to human skin, nontoxic on local application to large denuded areas for long periods of time; produce no adverse effect on healing, and the antibacterial activity should not be abolished by organic matter.

The present work has demonstrated that two of the five compounds studied, n-propyl-5-nitro-2-furoate and 5-nitro-2-furaldehyde semicarbazone qualify as efficient antibacterial substances which are nonirritating and nontoxic under conditions of local application and do not delay the healing process in wounds in rabbits. In addition, Neter has shown that 5-nitro-2-furaldehyde semicarbazone was effective in the treatment of wounds in rabbits infected with hemolytic streptococci.

As a result of these studies, 5-nitro-2-furaldehyde semicarbazone (designated as furacin) was deemed worthy of clinical trial. It was incorporated 1:500 in the washable base which was previously described for use on infected wounds in humans.

At the time of this writing, Snyder, Kiehn and Christophersen have prepared a preliminary report on a small series of cases of infected wounds treated with this preparation in which favorable clinical and bacteriological results were obtained and have recommended its further trial. They have also noted the lack of toxicity, irritation, and interference with healing which has been described in the present work on rabbits. Several other clinical trials are being conducted by McCollough and by Shipley who corroborate the earlier findings of Snyder and his associates.

Certain justifiable criticisms have been made recently of the experimental method used in this work as a valuable measurement of the healing rate of wounds. It has been pointed out by several workers that the method records chiefly the rate of contraction of the wounds and that it is not an accurate measurement of the rate of epithelization.

No attempt is made here to refute these criticisms, since the aim of this investigation was to provide as much information as possible with the

methods available on the properties of these compounds under conditions of continuous local application.

It is interesting to note, therefore, that the findings recorded here by the method of Carrel and Hartmann on the failure of 5-nitro-2-furaldehyde semicarbazone to interfere with healing were substantiated by the histological findings. It has also been shown by those investigating the clinical utility of this compound that epithelial grafts covered with it have consistently given excellent results and that no interference with the rate of epithelization was indicated.

SUMMARY

Five nitrofuran compounds of previously proved antibacterial activity were tested for irritation to human skin and for toxicity and effect on healing when applied to wounds in rabbits. Two compounds, n-propyl-5-nitro-2-furoate and 5-nitro-2-furaldehyde semicarbazone were found to be nonirritating, nontoxic, and have no adverse effect on healing under the conditions of the experiments. Because of its superior antibacterial activity, 5-nitro-2-furaldehyde semicarbazone has been recommended for clinical trial in infected wounds and preliminary trials show favorable clinical and bacteriological results.

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MALIGNANT LESIONS OF THE DUODENUM

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KNOWLEDGE gained in the performance of pancreatectomy and in the postoperative care of the patients is applicable to the surgery of malignant lesions of the duodenum and papilla of Vater. The circumvention of the difficulties involved in the partial removal of the pancreas and duodenum with provision for the re-establishment of biliary and alimentary continuity is the same for all three lesions.

PATHOGENESIS

The rarity of carcinoma of the small intestine has provoked extensive discussion (13). Like the fallopian tubes and the spleen, the small intestine is so infrequently the site of a primary malignant lesion that it prompts search for some factor causing refractoriness to malignant change. If some of the hypotheses of the causation of cancer are correct, duodenal malignant lesions should be common. Let us take trauma as an example. The horizontal or third portion of the duodenum lies over the third lumbar vertebra and therefore is exposed to trauma. The duodenojejunal flexure, where fixed intestine becomes free, is a frequent site of duodenal rupture. Looking for sites where chronic irritation is common, one finds that the duodenum is a retort that is constantly charged with acids, alkalis, enzymes, bile salts, cholesterol, and the things we eat and drink. Chronic duodenal ulcers and erosion around duodenal fistulas are evidence of irritative properties of the duodenal contents.

Advocates of the hypothesis of malignant degeneration in gastric ulcers must assume some inhibitory influence in the duodenum. In 3 of the cases studied in this paper the pathologist seemed to concur with Jefferson's opinion (15), drawn from 30 collected cases, that carcinoma of the duodenum may result from malignant degeneration in an ulcer (4). But it may be pointed out that carcinoma of the duodenum does not show the predilection for the first inch of the duodenum that characterizes duodenal ulcer, even though, like duodenal ulcer, it is more common among men than among women. Critical examination of Jefferson's case reveals that the lesion may have been a carcinoma from the very first. He assumed that, because the lesion was diagnosed as a benign ulcer by palpation and $2\frac{1}{2}$ years elapsed before the carcinoma was obvious, the lesion was originally benign. Examination of our cases shows that the patient may live for many years after gastroenterostomy for duodenal carcinoma. Even if every carcinoma in the first part of the duodenum resulted from a duodenal ulcer, the incidence of duodenal carcinoma is so small as compared with that of duodenal ulcer that only an infinitesimal percentage of duodenal ulcers would undergo malignant degeneration.

Duodenal mucosa makes contact with gastric mucosa, two pancreatic ducts and one biliary duct. The cells of Brunner's glands perforate the muscularis mucosae. Robertson has reviewed the difficulties that confound the diagnosis of carcinoma of the duodenum. He observed that Brunner's glands are extremely passive and do not undergo any special or prominent alterations under abnormal conditions. Brunner's glands are most abundant in the first few inches of the duodenum and in the tissue surrounding the papilla of Vater. Review of the literature on the few cases in which malignant changes have occurred in the cells of Brunner's glands reveals that paradoxically the only carcinomas arising unquestionably from the cells of Brunner's glands are questionable carcinomas. Robertson presented data on one case in which there was unorganized hyperplasia with cells showing hyperchromatism, irregular arrangement and occasional mitotic figures. Since then we have encountered a surgical case in which proliferative changes in the cells of Brunner's glands were great enough to suggest to some of the pathologists examining the lesion that it was a definite carcinoma (Fig. 1). This case is not included in this series because its status is open to question.

Then there is the possibility of malignant degeneration in heterotopic tissues (9). In 23.5 per cent of cases of aberrant pancreatic islands, the aberrant tissue occurred in the duodenum (6). Diverticula may contain ectopic pancreatic or gastric mucosa (8,27). In this respect it is interesting to note that in 3 of the cases in this series diverticula were present and in 1 case an aberrant pancreatic nodule was found. Polyps, adenomas,

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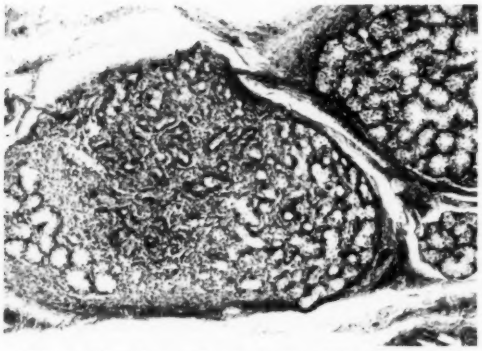


Fig. 1. Very low grade carcinoma of the duodenum in which the cells seem to have originated from the cells of Brunner's glands.

and papillomas may also undergo malignant change. It is surprising that carcinoma of the duodenum is not more common than it is. From our study we concluded that carcinoma of the duodenum may originate from any of the cells mentioned, but the bulk of the lesions represent anaplastic changes in the duodenal mucosa itself. If any of the processes mentioned contributed a considerable number of the lesions, this would be reflected by an increased incidence at the site of predilection of that process. In our series after exclusion of cases of carcinoma of the papilla of Vater the lesions were quite evenly distributed throughout the duodenum. Those who dismiss as imaginary the possibility of malignant change ever occurring in certain benign lesions of the duodenum must assume some extraordinary resistance conferred on the tissue by their presence (2).

The duodenum is rarely the site of metastatic lesions from other organs. Of course, as it progresses, carcinoma from the pancreas, because of its proximity, may perforate through the duodenum. No tissue will stop in very case the invasive growth of contiguous carcinoma. It is said that carcinoma of the stomach will stop short at the pylorus and carcinoma of the cecum will stop at the ileocecal valve but exceptions are encountered from time to time. Furthermore, such a lesion may stop abruptly at its contact with the small intestine and yet invade a loop of ileum or jejunum from without a short distance away.

Lieber, Stewart and Lund (17), Stewart and Lieber (26), and Berger and Koppelman have presented excellent reviews of reported cases of carcinoma of the duodenum. Bringing their figures up to date and including the cases presented here that have not been reported previously, one may state that 718 cases have been reported, of which 433 are acceptable. Considering that many cases are unreported, it is apparent that the lesion is not as rare as textbooks state it to be. Roughly, it occurs about 33 times in 100,000 necropsies (based on Eger's 350,286 collected necropsies) as compared with 3,000 times for carcinoma of the stomach. It comprises 0.3 per cent of intestinal carcinomas (12).

Because the cases in the literature are derived predominantly from postmortem material, we have avoided an elaborate analysis of the symptoms, which are usually terminal, representing the invasion of contiguous structures. This fact was demonstrated in several of the cases studied here, in which histories of the same patient taken a year or more apart by independent observers revealed how readily a patient forgets early symptoms when more distressing symptoms overshadow them.

MATERIAL FOR STUDY

There are 45 cases of surgical and 4 of nonsurgical malignant lesions of the duodenum in the records of the Mayo Clinic (15 of these cases have already been reported—11,16,20,24). In 13 cases the lesion was verified at necropsy. This study does not include carcinoma of the ampulla or papilla of Vater, which entails the possibility of lesions arising from the common bile duct, the ducts of Wirsung and Santorini, the ampulla or the papilla. Cases in which the pancreas was involved were omitted from this study unless the study of the edge of a slowly growing lesion revealed that it was of duodenal origin. Probably some cases of duodenal carcinoma are classified as pancreatic or vaterian, since at the time of examination the lesion has extended so far in some cases that its primary location cannot be ascertained. However, such cases must be credited to the more common lesion; that is, pancreatic or vaterian carcinoma. A brief analysis of the proved cases is presented here to elucidate some of the points of interest to the surgeon.

PATHOLOGY

In 44 of the cases the lesion was carcinoma of the duodenum. In 2 it was sarcoma, in 2 leiomyosarcoma and in 1 lymphangioendothelioma, which showed involvement of the regional lymph nodes. In 2 of the cases there were simultaneous independent gastric carcinomas and in 1 there was a synchronous lesion of the jejunum. In 3 cases a duodenal ulcer was coexistent and in 1 there was aberrant pancreatic tissue. Polypoid lesions were twice as frequent as ulcerated lesions. There have

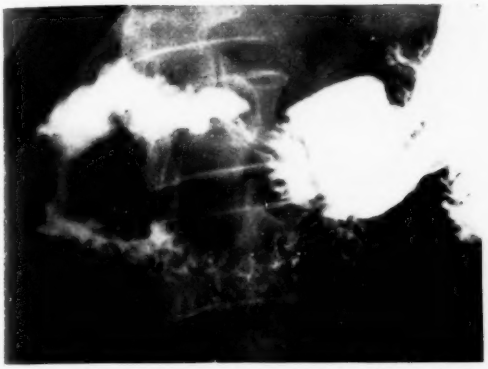


Fig. 2. Sharply demarcated constricting deformity in the descending (second) portion of the duodenum, with obliteration of the folds of mucous membrane in the deformed part. These features identify the lesion as a neoplastic one.

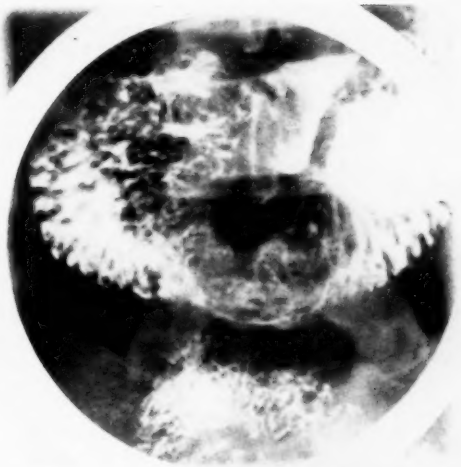
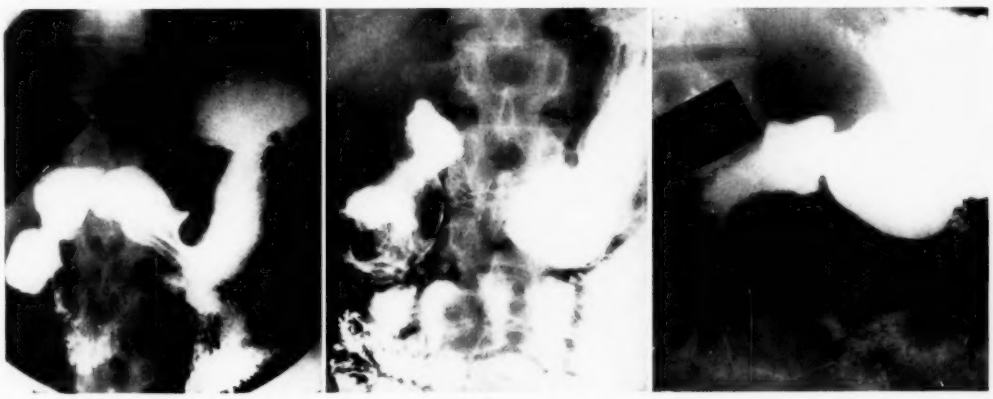


Fig. 3. Crescentic deformity in the horizontal (third) portion of the duodenum. The tumor was mostly intramural. The roentgenologic diagnosis was "leiomyoma."

been many attempts in the literature to attribute significance to the cylindric type of carcinoma or the spheroidal form, to hard scirrhous or soft medullary forms, but we found such distinctions of little value. As in carcinoma at other sites, the grade (Broders' method) of the lesion, the involvement of the lymph nodes and local or distant extension determined the prognosis.

INCIDENCE

Age. In the majority of the cases the patients were in the sixth or seventh decade. The average age of the patients who had carcinoma was 55.4 years. The youngest patient who had carcinoma was 26 years of age, 1 was 39 years, 8 patients were in the fifth decade, 18 in the sixth, and 16 in the seventh. The age of both patients who had leiomyosarcoma was 38 years. The sarcomas occurred at 17 and 64 years and the lymphangioendothelioma occurred at 27 years of age.



a b c

Fig. 4. Lesions of neighboring organs causing deformity in the duodenum. a, Carcinoma of the head of the pancreas extending into and causing ulceration in the duodenum and displacing it downward and toward the right side. b, Carcinoma of the hepatic flexure of the colon extending to and involving the duodenum. c, Lymphoblastoma of the retroperitoneal lymph nodes constricting a long portion of the duodenum without actually invading it. In all instances the extrinsic nature of the lesions was suspected at roentgenologic examination.

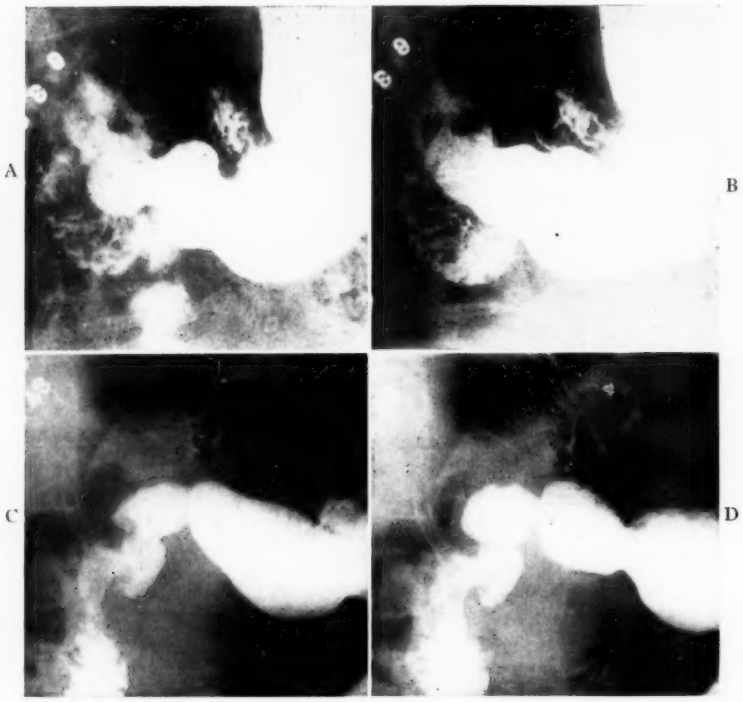


Fig. 5. a and b, Deformity of the first portion of the duodenum caused by primary carcinoma; the roentgenologic diagnosis was "duodenal ulcer." c and d, Deformity in the second (descending) portion of the duodenum caused by benign peptic ulcer; the roentgenologic diagnosis was "ulcerating lesion" but neoplasm was suspected.

Sex. Thirty of the patients who had carcinoma were men and 14 were women. The patients who had leiomyosarcoma were both men while the 2 patients who had sarcoma were women. The patient who had lymphangioendothelioma was a man.

Distribution. Fourteen of the lesions occurred in the first part of the duodenum, 15 in the second, and 20 in the third part. In collected series the greatest number is found in the second part. This is the result of the inclusion of vaterian carcinomas by many authors.

DIAGNOSIS

Because of their rarity, as compared with duodenal ulcers complicated by obstruction or bleeding, malignant lesions of the duodenum may frequently go undiagnosed. Experience at the clinic since 1938 has demonstrated that if both the clinician and the roentgenologist are on the lookout for such lesions, roentgenologic examination will be extended to include the entire duodenum and thus make a morphologic diagnosis possible. Many of the reviewers, following the lead of Pic, have devoted much effort to the differentiation by symptoms of lesions of the suprapapillary, peripapillary, and infrapapillary regions of the duodenum. They have gone into great detail, taking cases in which the lesion was discovered at necropsy, then going back and studying the record. We might say that one is doing well if one suspects the presence of a lesion of the pancreas, bile duct, or duodenum strongly enough to suggest that roentgenologic examination of the upper part of the gastrointestinal tract include the second and third portions of the duodenum. That is the way that definitive diagnoses were made in this series.

The symptoms of duodenal carcinoma are frequently present over a relatively long period. The average duration before admission was 11.8 months, with 2 patients giving a history of 6

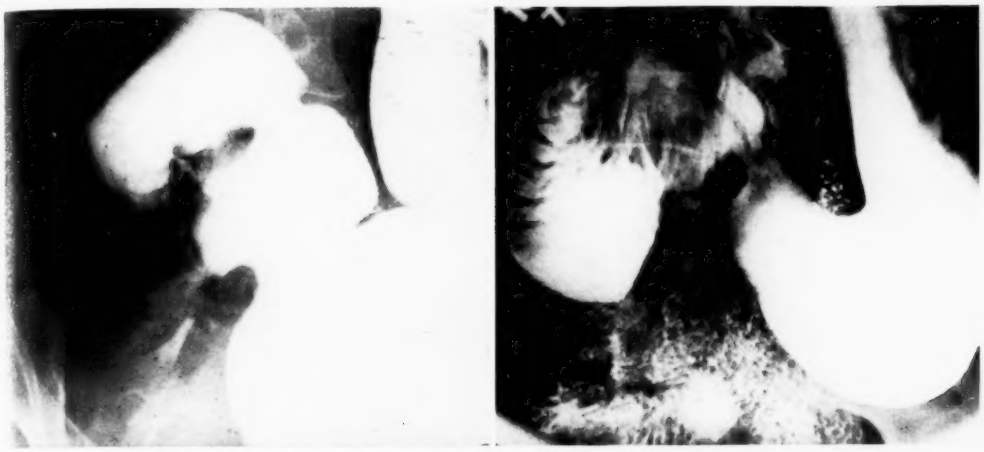


Fig. 6. Two examples in which carcinoma of the duodenum caused obstruction of relatively high degree. In a, left, the roentgenologic diagnosis was "obstructing lesion"; in b, the roentgenologic diagnosis was "carcinoma."

years' duration. In the cases studied here the symptoms appeared to be a result of the morphologic characteristics of the lesion rather than of its position. Four processes within the lesion seemed to account for the symptoms regardless of whether it was in the first, second, or third part.

Obstruction by a napkin ring stenosis or by an intraluminal polypoid lesion was most common. The latter type seemed to produce more cramps and borborygmi than the former. With long-standing obstruction there is dilatation of the stomach and duodenum and observing patients may note the splash of the gastric contents produced by gastric retention. The vomitus will contain bile in lesions of the third part but be clear in lesions of the first part. However, pressure on the bile ducts by lymph nodes may alter this.

Second, the lesion may ulcerate or slough, producing bleeding. The first indication of the disease to some patients is weakness and fatigue produced by anemia. Some of the patients seen in the early history of the clinic had been treated by their physicians for pernicious anemia for many months, but blood smears soon showed that the anemia was a result of chronic loss of blood. It has frequently been suggested that there is some defect in the absorption of the intrinsic factor (23) in cases of duodenal carcinoma, but loss of blood was demonstrated in all cases in this series in which there was anemia. No cases in which there was macrocytic hypochromic anemia were encountered in this series. This is understandable when one observes that a relatively small portion of the duodenum is involved by carcinoma. Meulengracht has suggested that the specific antianemic intrinsic factor is elaborated by the parts of the "pyloric gland organ," which is represented in the duodenum by Brunner's glands. In interpreting his hypothesis one should remember that hemopoiesis is not changed much after total duodenectomy and partial gastrectomy. The very low incidence of pernicious anemia after total gastrectomy is being studied now. Probably the critical test will come when total gastroduodenectomy is performed.

The third process that modifies the symptoms is perforation into the pancreas, in which case the pain of a pancreatic malignant lesion or pancreatitis may occur.

The fourth process that we wish to mention is obstruction of the biliary or pancreatic ducts. Carcinoma of the duodenum encroaching on the papilla of Vater will produce symptoms similar to those of vaterian or pancreatic carcinoma. One cannot assume from this that the lesion is in the second part of the duodenum, for involved nodes derived from a lesion of any part may cause jaundice, the first symptom, by pressure on the ducts. Occasionally there are points that aid in the differentiation. If the jaundice is preceded by signs of obstruction, one may suspect extension of a duodenal carcinoma. Intermittent jaundice favors the diagnosis of a duodenal lesion but a vaterian lesion may change its degree of obstruction by sloughing or reduction of inflammatory edema. Extrinsic involvement of a small segment of the common duct may produce obstructive

Fig. 7. Duodenum and part of jejunum and pancreas with the carcinoma of the duodenum.

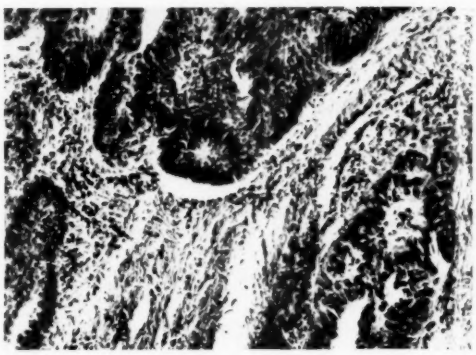


Fig. 8. Photomicrograph of carcinoma of the duodenum (×125).

jaundice even though a probe can be passed through the lumen easily at operation. In this series there was no case in which there was enough hepatic involvement to produce jaundice. In fact, the few metastatic regions in the liver that were seen were small.

Pain in the epigastrium or right upper quadrant of the abdomen was the most common chief complaint. It was present in 38 cases. It frequently began 1 to 4 hours after meals and was relieved by vomiting or sodium bicarbonate but not by food or milk. The onset was sudden in 6 cases and pain came on at night in 7 cases. The pain was usually steady but in 10 cases it was cramplike. The absence of extension of the pain was so uniform that when extension did occur one could assume perforation into the pancreas or obstruction of one of the ducts. Twenty-seven of the patients complained of bloating and belching. Gastric retention was advanced enough to produce frequent vomiting in 16 cases. In many of these cases the patients discovered that they could avoid retention by taking a liquid diet. In 4 cases retention vomiting had produced frank tetany with the concentration of chlorides in the region of 300 milligrams per 100 cubic centimeters of plasma, that of urea at 125 milligrams per 100 cubic centimeters of blood, and carbon dioxide combining power more than 70 volumes per 100 cubic centimeters of plasma (19).

In 6 cases the only complaint was of progressive weakness and fatigue. These cases presented a diagnostic problem until examinations of blood and stool revealed a bleeding gastrointestinal lesion. The concentration of hemoglobin was less than 6 grams per 100 cubic centimeters of blood in 17 of the cases and more than 13 grams per 100 cubic centimeters of blood in 12 of the cases. Hematemesis was present in 9 cases and melena in 12 cases. No portion of the duodenum showed a greater predilection for bleeding or obstructive lesions than any other.

Jaundice was present in 8 cases. It was a late manifestation in all except the 1 case reported later. In half of the 8 cases of jaundice, the lesion existed in the second part of the duodenum. In 3 cases it was in the first part and in 1 it was in the third part. Thus one cannot conclude that the lesion is periampullar in cases of jaundice. In the 222 cases of periampullar carcinoma of the duodenum collected by Lieber, Stewart, and Lund (18), jaundice was present in all but 4 cases. In 41 per cent (26) of cases of carcinoma of the supraampullar region jaundice was present. This greater incidence of jaundice in the collected series than in our series results from the fact that in almost all of the cases the patient was in the terminal stages of his condition when he was observed. In a large proportion of the cases in this series in which palliative operation was performed, jaundice developed shortly before the patient's death.

Alteration of frequency of evacuation or of consistency of the stools is not a common symptom in cases of carcinoma of the duodenum. The presence of typical diarrhea would make one suspect obstruction of the pancreatic duct. This is found in 35 per cent of cases of vaterian carcinoma (5).

Loss of appetite is not a common symptom among patients who have carcinoma of the duodenum. If one excludes the flatulence often present with gastric retention, only 2 of the patients complained of loss of appetite. One sees

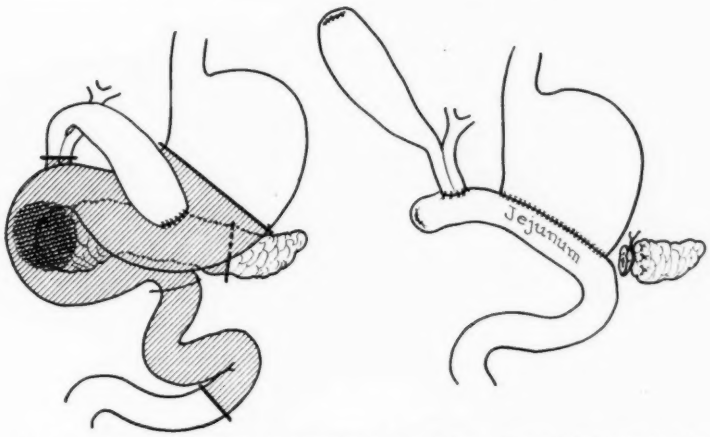


Fig. 9. Diagrams showing the situation of the lesion. The shaded area in the diagram on the left shows the extent of the region removed. The diagram on the right reveals the connections established between the biliary ducts and stomach and the jejunum.

similar situation among patients who have prolonged gastric retention after gastroenterostomy. They often complain of great hunger even when as much as 1,000 cubic centimeters of gastric contents is retained. In 16 of the 29 cases in which analysis of gastric contents was performed, anacidity was noted. The free acid content was high in 1 case, normal in 6, and low in 6. The average loss of weight in this series was 22 pounds (10.0 kgm.). The gall bladder was palpable in 2 cases. In 10 cases a mass was palpated in the upper part of the abdomen. In cases of carcinoma of the duodenum, the abdomen is usually flat and without gaseous distention.

ROENTGENOLOGIC DIAGNOSIS

Most reviewers state that a roentgenologic diagnosis of duodenal neoplasm is rarely made. Until relatively recent times this may have been true. However, that the roentgenologic diagnostic maneuvers, which have been used so successfully in the diagnosis of lesions in the esophagus, the stomach, the first portion of the duodenum and the large intestine, can be applied with almost equal success to the diagnosis of lesions of the small intestine is a fact that is becoming ever more widely appreciated. Weber and Kirklin reported on the experience at the Mayo Clinic with the roentgenologic diagnosis of neoplastic lesions encountered up to and including the year 1939. By then 17 instances of duodenal neoplasm had been encountered in which roentgenologic examinations of the duodenum were recorded. The existence of a lesion and its site were correctly predicted in all but 2 of the cases, although the precise diagnosis of neoplasm was offered in only 9 of them.

Since 1939, 20 cases of duodenal neoplasm have been encountered. In every instance the existence of the lesion and its location were correctly predicted at the roentgenologic examination. In 12 of the cases the roentgenologic diagnosis of neoplasm was later established at pathologic examination of the tissue (Fig. 2). In a single case of leiomyosarcoma of the third portion of the duodenum the roentgenologic diagnosis was ulcerating leiomyoma (Fig. 3). In 7 cases the roentgenologic diagnosis was given in such expressions as "lesion," "filling defect," "polypoid lesion," "intrinsic lesion," and "crescentic defect." Although not ideally precise, terms such as these have a connotation of neoplasm and so are considered to be satisfactory; a roentgenologic diagnosis can hardly be expected to be more precise than a gross pathologic one.

Tumors and other lesions of structures in close anatomic proximity to the duodenum sometimes extend to it and involve it segmentally, producing a roentgenologic picture similar in many respects to that produced by primary duodenal neoplasms. Cysts and tumors of the pancreas are especially prone to do this but tumors of the common duct near the ampulla of Vater, of the hepatic flexure of the colon, and of the retroperitoneal lymph nodes (Fig. 4) have also been known to simulate the roentgenologic picture of primary duodenal

lesions very closely. Evidence of the essentially extraduodenal nature of such processes is usually elicitable at roentgenoscopic examination, for such lesions tend to be large, and careful palpation almost always gives the clue to the correct diagnosis.

Obstructed hollow viscera are notoriously difficult to work with roentgenologically and the higher the degree of obstruction, the more difficult it is to determine the precise pathologic nature of the obstructing process at roentgenologic examination. Obstructing lesions of the duodenum are not exceptions, especially when the obstruction is encountered at or just below the pyloric ring. In this situation the roentgenologic evidence for neoplasm must be well developed, indeed, if a diagnosis of neoplasm is to be entertained, for in all age groups benign duodenal ulcer is overwhelmingly more often the cause of obstruction at this level than are neoplastic processes (Fig. 5). On the other hand, nonneoplastic obstructing lesions, intrinsic in the duodenum, are encountered comparatively rarely in the second and third portions of the duodenum. Therefore, it is expedient to consider neoplasm as a diagnostic possibility whenever obstruction is roentgenologically demonstrated to exist at these levels (Fig. 6).

Obstruction of all degrees was observed in this series of cases, the amount of gastric contents retained varying from 200 to 1,400 cubic centimeters. Efforts at reducing the amount of gastric retention by repeated gastric lavage fail as a rule to facilitate satisfactory roentgenologic examination, no matter what the cause of retention may be or where this cause may be located. The roentgenologic examination is hindered as much by the presence of gastric secretion as it is by the gastric dilatation. It seems that the mere act of passing the stomach tube increases the flow of gastric secretion in most cases and days rather than hours are consumed in reducing the size of a stomach dilated as a result of chronic obstruction. For this reason, operation is usually recommended as soon as the fact of chronic obstruction is established, because in the great majority of instances surgical intervention will become necessary no matter what the cause of obstruction may prove to be.

The roentgenologic criteria for the diagnosis of neoplasm of the duodenum are identical with those used in the diagnosis of such lesions in other tubular portions of the gastrointestinal tract. They have been adequately described in other publications and we have no additional data along these lines to describe.

At this point we wish to repeat a warning about the administration of barium by mouth to patients presenting symptoms of intestinal obstruction. When the obstruction is high in the duodenum, the clinical picture is clear enough to make the procedure safe. But lesions near the duodenojejunal juncture may present a clinical picture in which a lesion of the lower part of the intestine must be considered. In such cases it is wise to proceed with caution and aspirate the stomach and duodenum. A lesion of the colon should be ruled out before proceeding with the standard roentgenologic examination of the small intestine. Serious consequences have often followed the injudicious administration of barium by mouth to a patient who had a lesion of the lower part of the intestine. In such cases partial obstruction may be converted to total obstruction by barium.

SURGICAL ASPECTS

Up to 1935, unless a segmental resection in the first or third part or local excision was possible, lesions of the duodenum were not considered removable. Experience with resection of the pancreas and duodenum has changed the attitude, and radical resections are now possible. While it may not be possible to remove the node-bearing tissue of the periaortic chain, local extension on the surface of the pancreas can be removed by partial pancreatectomy. Applicable operative procedures, designed primarily for the treatment of pancreatic and vaterian lesions, have been discussed repeatedly by Whipple, Brunschwig, and Hunt.

It is difficult to assign credit for the greater present-day success in radical pancreatoduodenectomy to any single advance in surgery. Relatively little is known of the physiology of the duodenum. Even the fundamental functions of its cells are not clearly established. But it appears that men and animals can get along without a duodenum (7). On the other hand, the physiology of the pancreas has been the subject of careful study for a century. Early removals of part or all of the pancreas were performed with some knowledge of the disturbances created. Improved knowledge of the control of the electrolytes of the blood, the use of vitamin K, the availability of bank blood and plasma, the preoperative and postoperative administration of vitamins, carbohydrates and proteins to bolster the liver, chemotherapy and antibiotics have each played its rôle, so that a procedure that was impossible for the masters of the previous generation is within the scope of the young surgeon of today.

There is great variation of the individual requirement for the external secretion of the pancreas. Results obtained in animals cannot be applied directly. The necessity of anastomosing the ducts of a partially removed pancreas to the jejunum remains to be evaluated. The various methods for re-establishing the flow of pancreatic juice add materially to the risk of the operation. While it is the opinion of many surgeons that the flow of pancreatic juice is important, if not essential, we have encountered cases in which the patient did well after total pancreatectomy or partial pancreatectomy with ligation of the stump. In fact, some of these patients did well even without the oral ingestion of pancreatin. Furthermore, we have no knowledge of how long the pancreatic external secretion effectively continues after such anastomosis. Answers to these and other problems will be found only after larger numbers of cases in which radical pancreatoduodenectomy has been performed are available for study. When it is necessary to remove the entire pancreas, replacement of insulin is not difficult but the requirement of lipocaic, choline, or other factors in prevention of hepatic damage and infiltration with fat after long periods of survival must be evaluated for human beings.

There are manifold technical problems which arise during the performance of radical pancreatoduodenectomy. Many of these are concerned with the method of handling the common duct. In cases of duodenal ulcer with cicatricial stenosis and in those of carcinoma of the pancreas, ampulla, or first or second part of the duodenum, along with shortening of the duodenum, there is often a shortening of the common duct. This tends to draw on the fork produced by the juncture of the cystic and hepatic ducts so that the angle is reduced and the two ducts are fused side by side. We have encountered several cases in which use of the gall bladder for anastomosis was contemplated but in which, after ligation of what was believed to be the common duct, the surgeon found that in reality he was clamping the cystic and common ducts. These two ducts may run side by side to a point close to the duodenum. Thus a previously made cholecystenteric stoma, while it relieves biliary obstruction, may have to be disconnected during pancreatoduodenectomy because it is in the way and because when the common duct is tied, unless a probe is passed, there is no way of being sure how far the bifurcation is from the ligature.

In the performance of a palliative anastomosis of the gall bladder to the intestinal tract there are many advantages to cholecystojejunostomy for lesions in the region of the ampulla. If the gall bladder is anastomosed to the stomach and the patient survives for some time, the lesion may go on to obstruct the duodenum and the biliary flow will add to the vomitus. Hence it is better to anastomose the gall bladder to the jejunum than to the stomach. In 3 of the cases in this series, palliative cholecystenterostomy was followed by a subsequent palliative gastroenterostomy because the patient lived long enough to have duodenal obstruction.

Preoperative measures. So many vital functions are disturbed by lesions in the duodenum that extensive physiologic readjustments are necessary. Imbalance of electrolytes requires the intravenous or subcutaneous administration of sodium chloride and calcium. Anemia or hypoproteinemia makes blood transfusions essential. Determinations of prothrombin must be made to evaluate the need for vitamin K. Hepatic reserves must be bolstered by administration of carbohydrates and proteins. Intravenous administration of glucose is usually necessary to increase hepatic glycogen. Dilatation of the stomach must be reduced by repeated lavage.

During radical resections, which frequently involve more than 3 hours of operating time, intravenous administration of fluids is obligatory. In addition, the average patient requires at least 1,500 cubic centimeters of blood during and after the operation. Five to 8 grams of sulfathiazole should be dusted intraperitoneally. After radical resection it is usually wise to place the patient in an oxygen tent, administer blood, and maintain adequate blood levels of sulfadiazine and penicillin. Vitamin K should be added to the intravenously administered fluids, since biliary flow may be obstructed by edema.

REPORT OF A CASE

The following case illustrates some of the points stressed in this study.

The patient was a white woman 52 years of age. During the first week of January, 1943, she noted the sudden onset of a dull pain in the epigastrium "as if a lump was there." Belching and sour eructations were prominent. A week later she became jaundiced and pruritus was severe. Her appetite was good. It was believed that she had obstructive jaundice due to carcinoma of the pancreas. Severe hyperlipemia was present.

On February 3, 1943, cholecystogastrostomy was performed. The common duct and the gall bladder were dilated and a nodular mass was noted in the region of the pancreas. Biopsy of the liver revealed advanced infiltration with fat and cholangitis.

The patient was well for 1 year and then began to have severe epigastric pain, belching, and bloating. Her appetite was good but she lost 25 pounds (11.3 kgm.). At examination in January, 1945, there was no jaundice. The concen-

tration of hemoglobin was 8.9 grams per 100 cubic centimeters of blood and erythrocytes numbered 4,390,000 per cubic millimeter of blood. Analysis of gastric contents revealed anacidity. Roentgenologic examination of the stomach and duodenum revealed an obstructing lesion of the second portion of the duodenum with dilatation of the stomach and duodenum proximal to it.

On January 13, 1945, operation was performed. The entire duodenum, about 30 centimeters of jejunum and about two-thirds of the pancreas were removed. The cholecystogastric stoma was disconnected and choledochojejunostomy was performed. Half of the stomach was resected and gastrojejunostomy (posterior Pólya) was performed. During the procedure great difficulty was encountered in dissecting the pancreas free from the portal vein. Three small openings were made in the portal vein, and these were closed with fine silk. Figure 9 gives a rough diagrammatic approximation of the arrangement before and after operation. The shaded area depicts the region removed *en bloc*. The stump of the pancreas was closed by three catgut mattress sutures and left free in the peritoneal cavity. Passing from the patient's right to left the jejunum first received the biliary duct. The latter was represented by the biplicate cystic duct and hepatic duct, which looked like a single tube externally. Both were anastomosed end-to-side to the jejunum. The site of the previous anastomosis of the gall bladder to the stomach was sutured. The entire shortened common duct was found to have been removed with the specimen. The gastrojejunal stoma was made distal to the hepatojejunal stoma and the jejunum was sutured to the mesocolon at the site of the former ligament of Treitz.

The tumor was an adenocarcinoma of the duodenum, grade 1 (Broders' method), without involvement of lymph nodes (Figs. 7 and 8). The postoperative course was uneventful. For a short time the patient was mildly diabetic with a fasting concentration of sugar of 145 milligrams per 100 cubic centimeters of blood. She required 15 tablets of pancreatin (Wilson) three times a day to give her one or two solid stools a day. There was slight drainage from the incision for 3 weeks. When she was examined 6 months later, her blood was normal. She had gained 7 pounds (3.2 kgm.). There was no evidence of diabetes. She was well at the time when this paper was written—8 months after resection and 32 months after the lesion had been identified and considered inoperable at the first operation.

ANALYSIS OF OPERATIVE CASES

1. Combined duodenectomy, partial pancreatectomy, partial gastrectomy, partial choledochectomy and choledochojejunostomy was perfomed four times. There was 1 death in the hospital (25 per cent), which resulted from repeated gastric hemorrhages. The results in this group cannot be evaluated since the other 3 patients were alive when this paper was written 1 year, 7 months, and 3 months after operation.

2. Segmental duodenal resection with or without partial gastrectomy was performed four times with one death in the hospital (25 per cent). Here again the death was due to hemorrhage. Of the other patients, 1 died within 2 years while the remaining 2 were alive when this paper was written, 1 and 4 years after operation was performed.

3. Local excision was done in 1 case. The patient was alive 4 years after operation.

The remaining operations were palliative.

4. Posterior gastroenterostomy was performed twenty times with 4 deaths in the hospital (20 per cent). These patients were in very poor condition. In 2 instances the patients were unconscious as a result of gastric tetany and the operation was of an emergency nature. The surviving patients demonstrate that the lesion is frequently slow in progress when the obstruction is relieved. No doubt in some of the cases resection would have been performed if the patients had been seen recently. The average period of survival for this palliative procedure was 21 months, with 4 patients living 7, 6, 3, and 2½ years after the gastroenterostomy to account for the high figure.

5. Anterior gastroenterostomy was performed three times with no deaths in the hospital. One patient died in 1 year and another in 3 months. The third patient could not be located.

6. Duodenojejunostomy was performed three times with 1 death in the hospital (33 per cent). One patient died in 3 years and the other in 3 months.

7. Cholecystostomy was performed twice with 1 death in the hospital (50 per cent). The survivor died 7½ months after operation.

Thus there were 8 deaths in the hospital in 37 procedures—a mortality rate of 22 per cent.

8. Exploration only was done eight times with 4 deaths in the hospital (50 per cent). The average period of survival in the 4 cases was 5.6 months.

In reading the literature on carcinoma of the duodenum one gets the impression that the prognosis is very bad. However, most of the reported cases are taken from necropsy records. On the other hand, from the surgical cases presented here, one gets the impression that when radical duodenectomy is well established the results in cases of this rare lesion will be better. In the case presented earlier in this paper the lesion was resectable 2 years after it had been identified at a previous operation. While, in general, extension into the local nodes seems to occur relatively early, there is a long latent period before the lesion extends to distant sites such as the liver or lungs. The prognosis for lesions of the duodenum is better than for lesions of the jejunum or ileum. This may be explained by the proximity of the lesions of the duodenum to the stomach and the inclusion of two important ducts in the region, which tend to produce symptoms earlier. It is true despite the greater apparent ease of removal of lesions of the jejunum and ileum.

In the collected series in the literature it is stated that postoperatively the prognosis of lesions of the first and second parts of the duodenum is very poor. In this series 1 patient was alive when this paper was written, 6 years after resection of a lesion of the first part of the duodenum and another died 7 years after gastroenterostomy, at which time the lesion was confirmed by necropsy. In lesions of the third part of the duodenum the results are not as good, with only 2 patients alive 2 years after operation.

SUMMARY

Forty-nine cases of malignant lesions of the duodenum, exclusive of lesions of the papilla of Vater, are analyzed. Obstructive features were prominent in 38 while in 6 cases anemia resulting from loss of blood was the chief finding. In 45 cases operation was performed. Radical resection was done in 4 cases, segmental resection in 4, and local excision in 1. The operative mortality rate in cases in which procedures other than exploration were performed (37 cases) was 22 per cent.

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PILONIDAL SINUS—TREATMENT BY PRIMARY CLOSURE

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THE problem of pilonidal cyst or sinus has provided a challenge to military surgeons that is both annoying and baffling. The records of the Army and Navy provide parallel experiences with this lesion, some of which tax one's credulity. In the two war years of 1942 and 1943, 359,209 sick days were lost by navy personnel due to this disorder. One young man spent 16 consecutive months in a naval hospital cheerfully awaiting healing of a wide open wound resulting from excision *en bloc* of the diseased tissue. A second young man during 12 consecutive months underwent 4 operations for the excision of recurring sinuses. A third young man of 19 was inducted into the service with a cyst for which he had already been treated for 2 years, and he spent his first 12 months of service undergoing further treatment.

Recurrences in the individual cases may number from two to ten! And they may occur as late as 2, 3, or 5 years after the presumably successful operation for cure. The problem seems simple and yet it has resisted the ingenuity of a host of able surgeons (2), each of whom has his favorite, but sooner or later disappointing, method of treating this apparently trivial but disabling lesion.

Some alleged recurrences are more probably subcutaneous abscesses having their origin in abrasions of the delicate skin overlying poorly vascularized and therefore vulnerable scar tissue. In such instances there are no buried epithelial elements and no buried hairs. The following case illustrates this possibility:

G.J.Z., aged 31 years, was admitted to Naval Base Hospital 20 with an acutely inflamed area over the sacrum about 10 centimeters by 10 centimeters, of 2 weeks' duration. Ten years previously he had had an incision and drainage of an abscess over the lower sacrum followed 6 months later by recurrence, when it was first incised, then excised and closed by primary suture. He remained cured for 5 years, when inflammation with discharge of pus occurred, followed by healing and recurrences once or twice yearly. The present attack had begun 2 weeks previously with pain and subsequent copious discharge of thin pus. Physical examination revealed a fever of 102 degrees F, a draining sinus directly in the midline at the lower end of the previous excision, surrounded by a widespread sacral cellulitis with a marked inguinal adenopathy, bilateral pelvic pain, and tender iliac glands. Following sulfadiazine and penicillin therapy, the infection was effectively controlled, the wound healed, and he was returned to duty.

The opinions in this article are the private ones of the writer, and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

Presented before the Western Surgical Association, December 1, 1945.

True recurrences, on the other hand, are due invariably to buried epithelial elements overlooked or inadvertently left behind at the initial operation. The following enlightening observation serves to explain the inherent difficulty in avoiding such recurrences.

A sailor, aged 19 years, was admitted, with a deep dimple over the end of the coccyx which was known to have been present since birth. Occasional slight discharge and local tenderness had been the only symptoms. On examination a tuft of hairs was disclosed in the depths of the dimple establishing it as a true "nest of hairs," or pilonidal cyst. At operation, excision of the dimple and underlying tissues was carried deeply, just exterior to the precoccygeal and lower presacral fascia. To our amazement, inspection of the bared coccyx revealed a tuft of hairs still protruding directly from the bony part of the tip of the coccyx. The coccyx was isolated and excised and microscopic section disclosed the end of the hair-containing sinus within the substance of the bony coccyx (Fig. 1b).

Certain recurrences suggest the possibility that the burial of the epithelial elements capable of producing such hair-containing sinuses may be an *acquired* and not necessarily a congenital phenomenon. On several occasions, dimpling of the skin and a subcutaneous sinus penetrating the deeper tissues have occurred in the very line of scar of the previous excision, and it seems highly probable that invagination and burial of skin elements may occur during a prolonged healing process in which there is a downgrowth of epithelium below the level of the surrounding skin. This downgrowth of epithelium is encouraged by the common practice of strapping the buttocks together in the hope of encouraging healing. It is possible that the growth of hairs from the walls of this acquired dimple are directed inward, establishing a simple sinus tract in which hairs are deposited and destined to act as a foreign body for the perpetuation of the infection. Strongly pertinent evidence to support this theory was a recent observation in a patient who had already undergone four operations for excision of recurrent pilonidal sinuses. His last wound had healed except for a small dimple in the wall of which was demonstrated the root of a hair, the hair itself being directed through the dimple into the subcutaneous tissue to a depth of 4 centimeters.

Early in 1942, observations made at the Mare Island Naval Hospital indicated that the delayed

healing associated with excision *en bloc* of diseased tissues in the sacral area (7) might be ascribed to four factors inherent in this particular region of the body, all inimical to good healing and to control of infection, namely, moisture, heat, motion, and trauma. Moisture is ever present due to wound discharge and perspiration; heat is abnormally increased due to interference with the normal heat radiation from the skin surfaces of the buttocks normally contiguous and, in the presence of a wound, abnormally closely apposed by adhesive plaster. The constant motion of the involved buttocks during any exercise and the constant trauma of sitting are particularly inimical to healing in this area. Buie has aptly called it "jeep disease."

On the basis of these convictions, the patient with an open wound following wide excision who previously had been ambulatory but who could not be returned to duty until healed, was put to bed, was made to lie on his abdomen or side, and was forbidden to lie on his back or to sit down. Instead of drawing the wound edges together, the buttocks, and therefore the wound edges, were pulled apart by adhesive strapping starting at the wound edges and completely encircling the body. The wounds were left open to the air or were exposed to sun light or quartz lamp radiation for part of the day, and treated with azochloramid and, more recently, with penicillin compresses. Better control of infection was immediately evident, followed by the development of firm healthy-looking granulation tissue, which filled the bed of the wound and ultimately provided a well vascularized base across which epithelium could grow.

Certain other fundamental difficulties of healing, which are also considered as being inherent to this area, are encountered when primary closure of the wound following excision of the diseased tissue is attempted. It is obvious, for example, that because of the mobility of the buttocks, lack of skin to close the wound is rare. The trouble lies primarily with the dead space directly over the sacral and coccygeal fascia. The tendency in all excisions is to conserve skin and to direct the plane of incision mediolaterally (Fig. 2 C). Logically, however, excision should always be in the opposite direction, that is, in the lateromedial plane (Fig. 2B). Under the latter conditions, as the base fills in with granulation tissue, the mobile skin of the buttocks will gradually be pulled in by fibrous contraction and healing will occur. If, however, following simple excision, the skin is closed, as in Figure 2B, it is obvious that a dead space will remain, which fills with blood and almost inevitably becomes infected. Either complete breakdown of the wound occurs, or the skin heals over a subcutaneous abscess cavity or an infected sinus tract. This must be widely opened, since one of the fundamental laws of healing requires that when a bridge of skin overlies a granulating infected cavity or sinus in the same manner as a chord subtends an arc, the chord or bridge of skin must be divided before healing can be expected.

Many techniques have been evolved in the attempt to close this presacral dead space incident to excision of the cyst or sinus. Incisions undermining the fat laterally over the sacral and gluteal fasciae produce flaps of skin and fat which are drawn together by tension sutures of various ingenious designs, supplemented by pressure dressings. The objection to such devices is the poor healing qualities of fat when strangulated and devitalized by encircling ligatures or by pressure dressings. Avascular or dead fat provides a good culture medium for the growth of bacteria which gain entrance to the subcutaneous tissues by way of the tension sutures themselves when introduced through the normally dirty and contaminated skin of this area. Lateral incisions to permit approximation of fat and skin in the midline without tension and with less necrosis of the tissue included in the sutures has been tried and found wanting (Lahey). Other operators, despairing of closing this dead space satisfactorily, have resorted to primary skin grafting (Scarborough) or to marsupilization of the incised sinus to the edges of the skin (Buie), or to complete excision and fixation of the skin edges to the sacral fascia, leaving a small area for epithelization in a deep gutter (MacFee). These various methods have common faults: they result in tender delicate scars and irregularities of the healed surface, easily subject to trauma and recurrent infection. Moreover, many attempts at primary closure fail because of infection of the traumatized necrotic fat, resulting in prolonged healing of broad open wounds followed by tender vulnerable scars.

The method which I have found most useful and which has been evolved from experiences good and bad through the past few years, provides for mobilization of the fascia overlying the gluteal muscle (Fig. 2*D*) on both sides together with a thin layer of muscle tissue, and approximation of these mobilized muscle-fascia flaps in the midline. The mobilization of the fascia and muscle must be sufficient to permit approximation without tension (Fig. 3). Included in the sutures is a shallow bite of the presacral or precoccygeal fascia, thus insuring obliteration of the dangerous dead space. The principle of using the

gluteal fascia was first brought to my attention at the Mare Island Naval Hospital, in 1942, by Commander Charles E. Pope, then in charge of these cases. Miscall and Holder and F. C. Shute *et al.* have also described the use of the gluteal fascia but in a manner that entails approximation of these tissues under greater tension than the Pope procedure.

In the utilization of the gluteal fascia, certain details of management and technique have developed which are considered most important in achieving a successful primary closure:

1. As little trauma as possible is inflicted on all tissues. Even retractors are not used, so as to avoid injuring the delicate fat cells lining the wound.

2. Contrary to almost universal advice in recent articles, clamps on bleeding vessels are rigidly avoided! Patience and local digital pressure usually suffice to stop the bleeding, and rarely is it necessary to place any ligatures on bleeding arteries regardless of the forceful bleeding that follows the initial incisions, thereby reducing greatly the dead and traumatized tissue as well as the amount of foreign material left in the wound to interfere with healing. Our experiences with bleeding from divided arteries in this area substantiate the observation that a completely divided artery usually retracts into the tissues followed by cessation of bleeding. Frequently when bleeding persists, close inspection reveals that a tangential wound of an artery has been produced or a branch has been severed at a point flush with its emergence from the parent artery. An incision completely severing the artery at point of bleeding results in prompt cessation of bleeding.

Following excision *en bloc* of the diseased tissue the wound is packed lightly with gauze while the operator carefully explores the sinus tracts with a probe to determine if by chance any tract has been cut across leaving behind epithelial elements. If such oversight has occurred, wider excision is performed.

3. The interrupted sutures of No. 0 chromic catgut (Fig. 4A) approximating the fascia are minimal in number (4 to 8). The use of nonabsorbable sutures in this area was reluctantly abandoned after we had been compelled on a number of occasions to operate for the removal of buried sutures of cotton, silk, or wire placed there by others or by us. These sutures in the gluteal fascia serve also to bring together the overlying fat, so that no devitalizing and traumatizing sutures are applied in the subcutaneous fat. There are only two layers of suture: one approximating the gluteal musculofascial flaps and one closing the skin (Fig. 4C).

4. The skin is approximated by a special continuous subcuticular stitch of dermol or wire applied 2 to 3 millimeter within the epithelial edge (Fig. 4B). The two ends of the dermol protrude from the wound at either end without any tying of knots. Frequently, the length of the incision requires that 2 such continuous sutures be applied (Fig. 5C) which are not withdrawn until the 7th or 8th day. The use of the subcuticular stitch which is considered a most important detail avoids passing sutures through infected skin into vulnerable fat. Skin sutures in this area, if left in place for several days, show redness and inflammation around each stitch hole, indicating that bacterial organisms are present which could easily penetrate the deeper tissues and infect the wound.

5. No drains should ever be used in this area, but the superior or posterior end of the wound is not closed for about 2.0 centimeters so as to provide an escape for tissue fluid or blood. At first the skin at the *inferior* or *anterior* end of the wound was incompletely closed but experience early taught us that the skin in the gluteal fold must be approximated very carefully—epithelial edge to epithelial edge—otherwise a small granulating wound remains in the gluteal cleft which heals poorly because of heat, moisture, and motion. As previously stated, this delayed and prolonged healing deep in the gluteal fold may produce a dimpling or downgrowth of epithelial elements below the level of surrounding skin—a factor which may favor the penetration of hairs into subcutaneous areas and the recurrence of infection. The wound is dressed with gauze moistened with tincture of merthiolate or zephiran solution so as to inhibit bacterial growth if later soaked with blood. To relieve tension from the sutures approximating the gluteal fascia, the two buttocks are securely strapped and pulled together with long adhesive strips. The wound is not dressed for 7 to 8 days. If bleeding occurs sufficiently for blood to escape the gauze dressings during the first 24 hours, the original dressing is not removed but is simply reinforced with additional gauze placed over it. An order to that effect is left with the nurse.

6. Chemotherapy is utilized *before*, *at*, and *after* operation. For 24 hours preceding the operation, penicillin is administered in optimum dosage (20,000 units intramuscularly every 3 hours), plus sulfadiazine and sodium bicarbonate, 1 gram each, every 4 hours orally; at intervals during the operation, sulfanilamide is smeared into all nooks, crannies, and crevices of the wound (3), and the

Fig. 1. a, Patient with subcutaneous abscess and *eleven* midline dimples. b, Nest of hairs completely surrounded by bone of the coccyx necessitating coccygectomy for complete removal of the pilonidal elements. Failure to recognize such deep penetration of hairs undoubtedly is responsible for some recurrences.

newly created raw surfaces are moistened with penicillin solution—(50,000 units in 25 c.c. water; the balance of 50,000 units is administered intravenously). After operation the administration of penicillin and sulfadiazine is continued as described for 4 or 5 days.

7. The patient is returned to his bed with specific instructions: He may lie on his abdomen or on his side and may stand to void, but he may not lie on his back nor may he sit. He is confined to bed except for lavatory privileges.

8. A nonresidual diet is imposed for 7 to 8 days, thus reducing the need of bowel movements to a minimum.

9. Even though healing is complete in 10 days to 2 weeks' time, military personnel are not returned to full duty under 4 to 6 weeks, in order not to jeopardize the final result in any way. An occasional sequel of the operation is a temporary numbness of the midline skin due to division or to temporary physiological block of subcutaneous nerve fibers incident to the mobilization of the gluteal fascia. This is usually not a subject for complaint, and gradually disappears.

When large subcutaneous abscesses have burrowed their way over the upper sacrum, the procedure described must be modified. The gluteal fascia is mobilized as here described to cover the coccygeal and lower sacral area. Over the upper sacral area where healing more readily occurs and where raw areas are not subjected to factors inhibiting healing as in the deep gluteal folds, the skin flaps are tacked down directly to the presacral fascia (5) by interrupted sutures of fine catgut including a bite of the fascia and a bite of

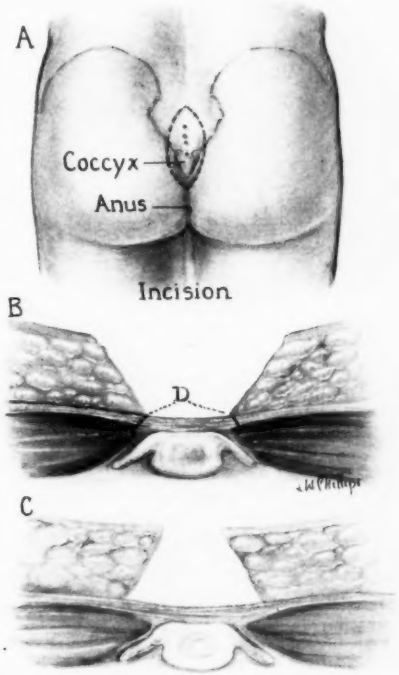
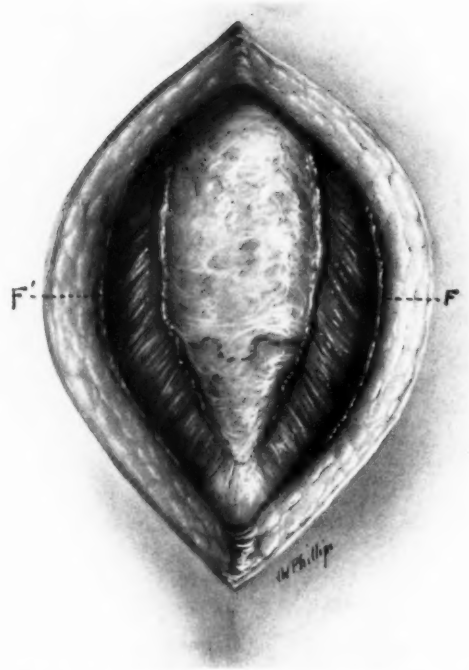


Fig. 2. A, Elliptical incision through skin and subcutaneous tissue. B and C, These incisions should be directed lateromedially and *not* mediolaterally to avoid undermining of skin and formation of an incollapsible dead space over coccyx and lower sacrum. *D*, Lines of incision in gluteal fascia which will permit its mobilization and approximation in midline.



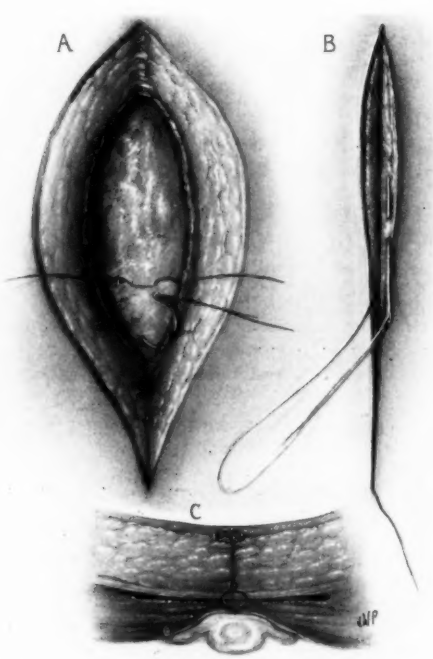


Fig. 3, left. Mobilization and lateral displacement of musculofascial flaps, *F* and F^1, which will be united in midline overlying the coccyx and lower sacrum.

Fig. 4. A, Approximation of musculofascial flaps by four to eight interrupted chromic catgut No. 0, including also a bite in the midline of the precoccygeal or presacral fascia, thus insuring obliteration of the dreaded dead space. B, Approximation of skin is effected by continuous subcuticular sutures of dermol or steel which are not tied, and which after 8 to 9 days are completely withdrawn from the wound. The skin in the posterior 2 centimeters of the wound is not closed by sutures but is left open for the escape of blood and serum. C, Only two layers of sutures are necessary—one in the gluteal fascia which also approximates the fat, and a second layer in the subcutaneous tissue.

subcutaneous tissue about 1.5 centimeters lateral to the skin edges. The skin edges may or may not be approximated by a subcuticular stitch of continuous dermol, leaving the superior 1.5 to 2.0 centimeters of the wound open. When the skin is not closed, there is usually only a small granulating area present as in the MacFee procedure which heals in a short time. Occasionally, the subcutaneous hair-containing abscess cavity extends anteriorly from the coccyx to a point lateral to the anus. After excision this lateral wound may be left either open or closed primarily.

When this method of closure fails, the wound is converted into an open one and treated as previously described for open wounds in this area. Despite failure of primary union it has been observed that the mobilization of the gluteal fascia permits more rapid cicatricial contracture of the wound, and healing is not as prolonged as in the usual excision *en bloc* and open method of treatment.

As experiences with the method described have led to such modifications as the elimination of skin-penetrating sutures, the use of the subcuticular stitch, and the local and systemic administration of sulfonamides and penicillin, failures have definitely decreased. In the last 46 cases there have been 5 failures, 2 due to hematomas which required evacuation, resulting in delayed but not prolonged healing, and 3 due to infection, one with a pyocyaneus infection that did not yield to penicillin and sulfa therapy, and one whose sinus involved the margin of the anus. It should be freely admitted that in the search for a dependable treatment of pilonidal cysts and sinuses, the methods used by many operators have been found successful some times, even

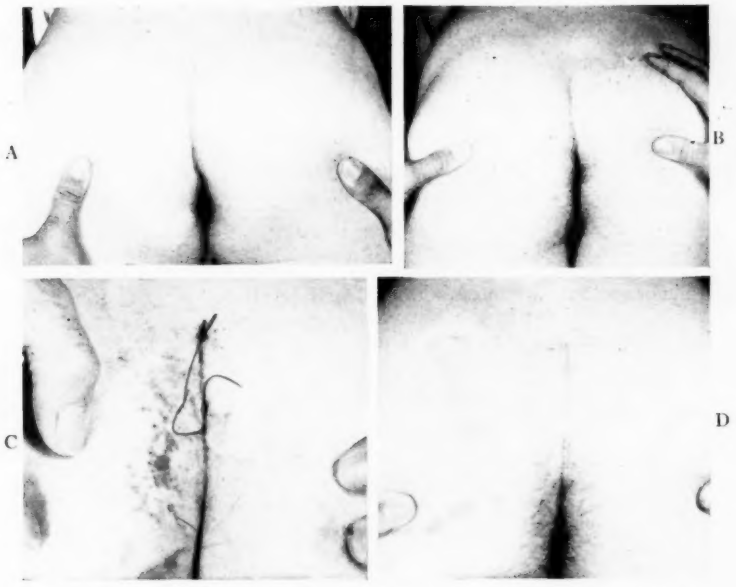


Fig. 5. a, Postoperative appearance in patient 1 on 10th day. b, Postoperative appearance in patient 2 on 12th day. c, Postoperative appearance in patient 3 on 7th day before removal of two dermol continuous sutures; the protruding suture is cut off at one end and pulled out of tissues by traction on other end. The dark area at posterior end of wound represents the 2 centimeters long unsutured area through which blood and serum can escape during first 48 hours after operation. d, Postoperative appearance in patient 4 on 14th day.

many times, but failures annoyingly recurred. It may be that careful attention to certain details, which to some may seem minor, will assist in the attainment of the perfection that we seek. It is confidently asserted that in the treatment of this lesion by primary closure, the attention to such minor details is often the determining factor between success or failure.

SUMMARY

Among military personnel, pilonidal cysts and sinuses have provided a problem of major importance. Following the block dissection—open wound treatment, healing and convalescence are prolonged, and recurrence remains an annoying problem.

There are four factors inherent in the lower sacral and coccygeal area which interfere with proper healing, and are conducive to prolonged and ill controlled infection, namely, moisture, heat, motion, and trauma. In the postoperative care of open wounds following block dissection, the following points are stressed: (1) rest in bed, (2) spread rather than approximation of buttocks accompanied by exposure of wound to sunlight or Quartz lamp radiation, and (3) instructions forbidding walking, sitting or lying supine until the wound is healed.

The re-establishment of typical midline dimples in the line of scar following block excision suggests that this lesion may be acquired as well as congenital in origin. Downgrowth of epithelium below skin level and penetration of deeper tissues by growing hairs during the prolonged healing process may be the cause of such recurrences.

In attempts at excision and primary closure, the greatest stumbling block to good healing is the dead space between skin and sacral and coccygeal fascia.

The most dependable method of primary closure utilizes gluteal muscle-fascia flaps according to the method of Pope, rather than subcutaneous fat to fill in this dead space. Following their mobilization for several centimeters lateral to each lateral edge of the coccyx and lower sacrum, the gluteal musculofascial flaps are approximated in midline by a minimal number of chromic catgut No. 0 sutures including also a bite of the pre-

coccygeal and presacral fascia in its lower half. The skin is approximated by 1 or 2 continuous subcuticular stitches of dermol or steel wire which are removed in 7 to 8 days. The skin is left open for 2 centimeters at its upper or posterior end to permit escape of wound fluid and blood. Drains into the wound must *not* be used.

Chemotherapy including administration of penicillin and sulfadiazine is utilized before, at, and after operation.

Operation is performed with the least possible trauma to tissues: Blood vessels are not crushed, clamped, nor tied in order to reduce to a minimum foreign material and dead tissue in the wound. Fat is not devitalized by encircling sutures. The less trauma produced in the wound, the better healing and the less infection there will be in this highly vulnerable area.

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THE USE OF PENICILLIN THERAPY IN CONJUNCTION WITH FREE BONE GRAFTING IN INFECTED AREAS

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AMONG the early favorable results obtained with the use of penicillin in the control of infections involving bone, in the University of California Surgical Services, were 2 cases of subsiding acute hematogenous osteomyelitis (hemolytic Staphylococcus aureus), in which there was rapid revascularization and incorporation of sequestra in the process of healing of the bone. One case was observed in which a recently infected (hemolytic Staphylococcus aureus) Hibb's fusion of the spine containing free iliac bone grafts healed rapidly with penicillin therapy and remained healed without loss of the grafts. These experiences suggested the possibility of bone grafting in areas in which there was chronic infection, or in recently healed contaminated bone defects.

During the past year, 8 patients with infections of the bone in which free bone grafts have been implanted into infected areas have been studied. This study is part of the contract with the Office of Scientific Research and Development for investigation into the use of penicillin in the treatment of bone infections, under the chairmanship of Dr. Howard C. Naffziger, responsible investigator, at the University of California Medical School. The work described herewith has been done in collaboration with the orthopedic surgical services of Dr. LeRoy C. Abbott. Six patients had infected fractures with nonunion that involved the tibia and fibula; one patient had an infected fracture with nonunion of the femur, and one patient had tuberculosis of the knee associated with secondary infection involving the upper end of the tibia, the lower end of the femur, and the knee joint. In all cases the infection was in a chronic or quiescent phase when treatment was undertaken. The pathogenic bacteria cultured from these cases were hemolytic Staphylococcus aureus in 4 cases; Escherichia coli and hemolytic Staphylococcus aureus in 1 case; and beta hemolytic streptococcus and hemolytic Staphylococcus aureus in 2 cases.

Systemic penicillin treatment was given every 3 hours by the intramuscular route preoperatively in 5 cases. In 2 cases the preoperative dosage was 100,000 units per day for 4 and 6 days, respectively. Sulfathiazole was also given in one of the cases in which there was a combination of Escherichia coli and hemolytic Staphylococcus aureus in the wound. In 1 case the preoperative penicillin dosage was 150,000 units daily for 5 days; in another case 200,000 units of penicillin were given for 1 day before the bone grafting operation. One patient received 100,000 units daily for 37 days and 150,000 units for 5 days before the bone grafting operation. Three patients had no preoperative penicillin therapy.

In 5 cases the bone grafting operation was done in a field in which there were open infected draining wounds or sinuses. In the other 3 cases the grafting was done in areas in which infected wounds had closed recently. All of these patients had had previous operations and were incapacitated with an extremity that was useless because of infection or nonunion, or both. Three of these patients had previously had metal plates inserted for fixation; one of these had been plated twice. In these cases the old plates were removed before the bone graft was inserted. A wound cleaning and trimming procedure had been carried out on all the patients with compound fractures at the time of injury. A "saucerization" had been done without benefit in one case. A previous attempt at free bone grafting in conjunction with sulfa therapy had been made in one patient, but the graft was lost because of infection. The patient with the secondarily infected tuberculous knee joint had had an arthrodesis of the knee joint and a synovectomy at previous operations.

The free bone grafting operations done with penicillin therapy were: (1) insertion of iliac grafts and metal plates, 4 cases; (2) sliding bone graft and metal plating, 1 case; (3) iliac grafts without metal fixation, 2 cases; and (4) sliding graft without plating, 1 case. The bone grafting was done in patients with infected wounds or

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The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development, Washington, D.C. and the University of California.

sinuses in 5 cases, and in closed but recently infected wounds in 3 cases. The wounds were closed completely in 7 cases, and in 1 case the wound was closed around a small rubber tube through which penicillin was given locally. The incisions used for the bone grafting operations healed *per primam* in 4 cases, but in 1 of these an adjacent sinus, which had been healed previously, reopened and drained for a time; 1 of these patients had a recurrence of infection after remaining healed for 6 months. She has returned for further treatment and possible removal of the metal plates. One patient who developed an infected wound that required opening for drainage was not included in this project at the time; she had received only 20,000 to 40,000 units of penicillin daily postoperatively for 7 days. Her wound healed promptly after she had received larger doses of penicillin and an incision for drainage; after prolonged penicillin therapy (3,550,000 units over a period of 32 days), it remained healed. Two wounds developed necrosis followed by low grade chronic infection of the soft tissues as a result of tension at the site of closure. Both of these open wounds were treated locally with daily dressings of penicillin ointment (500 units per gram) while being prepared for secondary closure or a skin grafting procedure. In 1 of these cases it was necessary to remove the metal plates, and at that time the bone graft was observed to be viable, well vascularized and firmly fixed in its position. At the time of this report, all bone grafts in the 7 cases of infected fractures appear by x-ray examination to be viable and in proper position, but one of the iliac grafts was fractured 4 months after its insertion. None of the grafts has sequestrated, extruded, or been absorbed. At present, the wounds of the soft parts are closed completely in 6 of these cases; they are open in 1 patient who developed a recurrence of infection after having had his wound healed for 6 months. Four of these patients have firm union of their fracture sites with metal fixation plates still in position, and 2 have firm union without metal plates. One patient mentioned previously, who obtained firm union without metal plates, fractured his graft 4 months after its insertion; he now has motion at the fracture site, for which a fibular transplant is being done. The wound of the patient who had iliac grafts placed in the bone defect following removal of the secondarily infected tuberculous knee joint has not yet been seen because the operation was done in November, 1944, and it will be necessary to immobilize the extremity for some additional time before the plaster can be removed for inspection. However, so far, no signs of infection have been observed.

Postoperative penicillin therapy was given intramuscularly at 3 hour intervals in all cases. The postoperative dosage in most cases was 100,000 units per day, and in cases in which operations subsequent to the bone grafting were necessary, several courses of penicillin were given, i.e., all secondary closures, skin grafting procedures, and fibular transplants were accompanied by a course of systemic penicillin therapy. In 2 cases in which the wounds separated because of necrosis of the soft tissues resulting from closure under tension, the infection was first controlled with the systemic therapy, then the wounds were kept clean with local dressings of ointment containing penicillin over the long period of 53 and 60 days, respectively, while waiting for favorable conditions for secondary closure or skin grafting. The total amounts of penicillin used so far in these cases have been from 3,760,000 to 9,700,000 units.

In addition to the 8 cases that have been studied under this contract with the Office of Scientific Research and Development, the orthopedic surgical staff has done 5 other bone grafting operations in contaminated bone defects, using penicillin therapy. The wounds of 4 of these patients have healed. In the 5th case the defect of the soft tissues was too large to permit closure of the incision and some of the bone grafts have been lost from the central part of the defect. This loss may be explained partially by the fact that systemic penicillin therapy has not always been given regularly and the wound may have been contaminated.

The period of observation of these cases has been too brief to permit final conclusions with regard to length of hospitalization and postoperative convalescence associated with the use of penicillin in combination with free bone grafting in the repair of infected bone defects. However, this preliminary study indicates that it may be possible, with these methods, to expedite considerably the recovery of some patients with infected fractures with nonunion.

At present it appears most desirable to obtain preliminary healing of the soft parts over infected bone defects with penicillin therapy, either alone or in combination with an operation for removal of sinus tracts, infected scars and granulations, and nonviable bone, and with skin grafting if necessary. Soon after the soft parts are healed, a bone grafting operation may be accomplished with a minimum risk under a course of preoperative and postoperative penicillin therapy. Our

experience indicates, however, that penicillin therapy makes it possible to obtain successful free bone grafting directly in bone defects infected with organisms susceptible to penicillin in which it may be undesirable to wait for preliminary healing. The use of metal devices for internal fixation may be necessary in some of these cases, but they should probably be avoided in contaminated areas unless they are absolutely indispensable to maintain fixation and position. If they are used, it may be desirable or even necessary to remove them after firm union of the bone has been obtained.

In cases in which free bone grafting is done in a contaminated area, penicillin therapy should be regulated with bacteriological studies, including identification of the bacterial flora of the wounds, with frequent cultures and tests for sensitivity of the organisms to penicillin. The presence of penicillin-resistant nonpathogenic organisms has not interfered with free bone grafting in a contaminated bone defect, provided the pathogenic organisms were sensitive to penicillin; however, penicillin-resistant organisms often delay healing in open wounds in the overlying soft tissues.

In cases of bone grafting, the systemic penicillin therapy has been given intramuscularly at 3 hour intervals. It is probably safest to precede the bone grafting operation by at least 3 to 7 days of systemic penicillin therapy. Experience with such cases as well, as with the treatment of other infections of the bone, indicates that postoperative treatment with penicillin should be prolonged for several weeks—usually from 3 to 8 weeks, depending somewhat on the type of organism, the amount of contamination, and the size of the area that must become revascularized during the period of healing after infection is controlled. The dosage of penicillin also varies somewhat with these conditions and should probably be at least 100,000 units daily under the most favorable circumstances, and up to 200,000 units daily, or more, in others. Where the contaminated area is accessible to local penicillin therapy, it appears desirable to instill from 5,000 to 30,000 units daily through a small soft rubber tube, for 7 to 14 days postoperatively. The strictest asepsis should be practiced in handling and injecting the penicillin solution into the tubes. They should probably be removed from the wound by at least the 14th postoperative day, by making a small circular opening in the cast around the tubes. All secondary operations, such as those for delayed closure, removal of plates, or skin grafting, should be accompanied by systemic penicillin therapy for several days before and after the operation.

Primary closure of the soft parts over the grafted bone defect is most desirable. It is reasonably safe and practical if cultures reveal the absence of penicillin-resistant pathogenic bacteria and if it can be accomplished without tension. Primary closure around a small soft rubber tube through which supplementary penicillin is given is even more advantageous when this is technically possible. The presence of penicillin-resistant nonpathogenic organisms does not ordinarily prevent closure and healing, but such bacteria may contribute to the delay in healing of open wounds in the soft tissues. Following operations in areas in which there are penicillin-resistant, potentially pathogenic organisms such as proteus, the wound in the soft parts should always be left open and secondary closure done several days later. In other cases, extensive soft tissue defects may necessitate skin grafting. In all cases in which delayed closure after bone grafting is necessary, it is essential that the wound be protected from contamination from external sources. Such areas should be dressed infrequently and with the strictest aseptic precautions.

Following are summaries prepared from the records of these cases:

CASE 1. A man, aged 43, had a fracture of the tibia for which an open reduction, followed by insertion of metal plates, was performed. The wound became infected and drained for 7 months before he entered the hospital in June, 1944, for penicillin treatment. The fracture site was not united. Bacterial cultures from the wound grew Escherichia coli and hemolytic Staphylococcus aureus. He received 100,000 units of penicillin intramuscularly daily for 2 days before operation, together with sulfathiazole. The first operation under penicillin therapy consisted of removal of the old metal plate, excision of sinuses and infected scar tissue. The wound was closed without drainage. Postoperatively 100,000 units of penicillin were given daily for 21 days, and sulfathiazole treatment was also continued for this period. The wound apparently healed *per primam*, but 8 days after the administration of penicillin was discontinued, a small area of infection developed and the drainage again contained Escherichia coli and hemolytic Staphylococcus aureus. A second course of penicillin, 100,000 units daily for 15 days, without sulfa therapy, was given and the wound healed promptly and remained healed. The patient was discharged with plaster fixation for 2 months, after which he returned to the hospital on August 10, 1944, for a bone grafting operation. The wound had remained healed, but there was nonunion at the fracture site. Preoperatively penicillin was administered at the dosage of 100,000 units daily for 4 days. The operation consisted of insertion of a free iliac bone graft with metal plate fixation at the site of the nonunited fracture of the tibia. Postoperatively 100,000 units of penicillin were given daily for 7 weeks. The wound through which the bone grafting was done healed *per primam* and remained healed. However, the old sinus tract was opened during the manipulation and it began to drain on the 10th postoperative day. Cultures grew Escherichia coli and beta

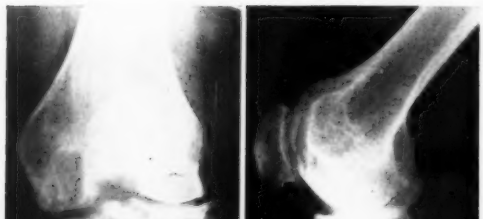

Fig. 1. Case 5. X-ray appearance of left knee of patient with tuberculosis secondarily infected with hemolytic Staphylococcus aureus.

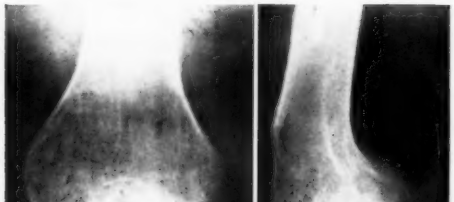

Fig. 2. Case 5. Condition present 3 months after excision of infected joint and insertion of bone grafts under penicillin therapy.

hemolytic streptococcus and diphtheroids. This wound closed gradually and was completely healed by the 28th postoperative day. The patient left the hospital on crutches, with the extremity in plaster, 55 days after entry for the bone grafting operation. His most recent follow-up visit was on February 6, 1945. The wounds have remained healed and there is no motion at the fracture site. Roentgenograms show evidence of repair of the fracture site. At present this patient has full weight-bearing without support.

Case 2. A man, aged 46 years, had an infected fracture of the femur with nonunion of 2 years' duration. There had been 2 unsuccessful attempts at internal fixation with metal plates. He entered the hospital for penicillin treatment on July 10, 1944. Hemolytic Staphylococcus aureus and Streptococcus viridans were cultured from the sinuses that drained from the ununited fracture site. He was given 200,000 units of penicillin preoperatively for 1 day. The operation consisted of removal of the old metal plate, excision of sinus tracts, scar and nonviable bone, and insertion of a free iliac bone graft and new metal plates. The wound was closed without drainage. Postoperatively the patient was given 200,000 units of penicillin for 1 day and 100,000 units daily for 17 days. The wound healed *per primam*, and he was discharged with crutches and wearing a brace, after 3 months' hospitalization.

Six months after his operation he developed a small draining sinus from which anaerobic streptococci were cultured. At present he has firm union, and he has reentered the hospital for another course of penicillin therapy and possibly removal of the metal plates.

Case 3. A man, aged 37 years, had a compound fracture of the tibia and fibula 3½ years ago, with chronic infection following an operation for internal fixation with metal plates. Subsequently the plates were removed and a "saucerization" performed and sulfathiazole therapy given, but the wound continued to drain. This patient entered the hospital for penicillin treatment on July 23, 1944, with nonunion of the fractures and an open, granulating wound from which hemolytic Staphylococcus aureus was cultured. Preoperatively 100,000 units of penicillin were given daily for 6 days. At operation, the sinuses, granulations, and infected scar tissues were removed, and a free iliac bone graft and metal plates were inserted. The wound was closed. Postoperatively 100,000 units of penicillin were administered daily for 47 days. The wound developed necrosis followed by a low-grade infection due to tension and too great undermining of skin flaps at the site of closure. After the wound became clean, bacteriostasis was maintained with penicillin ointment applied locally for 5 days. On December 18, 1944, the metal plates were removed, and the bone graft was observed to be viable, securely fixed in its position, and well vascularized. The patient received 100,000 units of penicillin daily for 10 days following this procedure. The open wound was covered with an intermediate thickness skin graft on January 12, 1945. The patient left the hospital on June 20, 1945, ambulatory, with an ischial weight-bearing brace. Apparently he has firm union at the bone-grafted fracture site and the skin is healed.

Fig. 3. Case 5. Six months after excision of infected knee joint and bone grafting under penicillin therapy. Wound healed *per primam*. Patient ambulatory with a stable knee joint.

CASE 4. A woman, aged 26 years, had a compound fracture of the tibia and fibula that failed to unite. On July 2, 1944, a sliding bone graft (tibia) was performed and metal plates were inserted. The patient, who was not included in this research project at the time, received from 200,000 to 400,000 units of penicillin daily for 7 days following the operation. At first the wound appeared to heal *per primam*, but a chronic infection developed subsequently. She entered the hospital on September 10, 1944, for penicillin treatment with two draining sinuses from which hemolytic Staphylococcus aureus was cultured. Before operation she received 100,000 units of penicillin daily for 3 days. Operation consisted of an incision for drainage; the bone graft and the metal plates were left in place. Postoperatively, she received 100,000 units of penicillin daily for 3 days, then 50,000 units for 7 days. On the 12th day of penicillin therapy the wound became sterile, healed promptly and has remained healed except for the extrusion of a single cotton suture. On February 15, 1945, there was a small crusted granulating area .5 centimeter in diameter, but no drainage. The patient has union and is bearing full weight on the extremity.

CASE 5. A man, aged 25 years, entered the hospital for treatment with penicillin on November 12, 1944. He had chronic osteomyelitis involving the left knee joint, tibia, and femur, of 20 years' duration. A diagnosis of tuberculosis was made 11 years previously, and a synovectomy was performed. The patient developed pain and swelling in the joint 1½ years ago, and an arthrodesis was carried out. Following that operation, persistent draining sinuses developed below the patella. Cultures yielded hemolytic Staphylococcus aureus. Preoperative treatment was 150,000 units of penicillin daily for 5 days. Operation consisted of excision of the knee joint, including infected bone from the upper end of the tibia, patella, and medial condyle of the femur. The defects in the bone were filled with bone grafts from the ilium, and the extremity was immobilized with pins in a plaster cast. The wound was closed around a small soft rubber catheter and penicillin, 10,000 units a day, was instilled locally for the first 8 postoperative days. Systemic penicillin, 150,000 units per day, was continued for 29 days postoperatively. The postoperative course was febrile to 102 degrees F. for several days, and then subsided to normal. Cultures obtained by aspirating the tube on the 9th postoperative day were sterile. Patient left hospital in a cast. The wound has not yet been inspected.

CASE 6. A man, aged 39 years, received a compound fracture of the tibia in August, 1943. It became infected and union did not take place. Under sulfa treatment, an operation for removal of nonviable infected bone and insertion of a free iliac bone graft was done, but it was not successful and the graft was lost because of infection. The patient entered the hospital for penicillin treatment on May 8, 1944, with an open draining wound on the lower leg and nonunion of the fractured tibia. Bacterial cultures grew hemolytic Staphylococcus aureus. Penicillin treatment was given as follows: 100,000 units daily for 15 days; 150,000 units daily for 5 days; 100,000 units daily for 22 days. The infection was controlled and the wound decreased in size, but it did not close completely. After 42 days of penicillin treatment, operation was performed. The old metal plate was removed. A free iliac bone graft was inserted at the fracture site. The penicillin was continued postoperatively, 100,000 units daily for 7 days. The wound healed, and the patient left the hospital 3 months after the operation. He accidentally fractured the bone graft 4 months after the operation and entered the hospital on December 12, 1944, for a fibular transplantation. The wound had remained healed, but clinical and x-ray examinations revealed that the bone graft was fractured.

Preoperatively he received 100,000 units of penicillin for 1 day, and the first stage of the fibular transplantation was carried out. This was followed by 100,000 units of penicillin daily for 17 days. The wound healed *per primam*. At present the patient is convalescing from the second stage of the fibular transplantation, which is accompanied by a course of penicillin.

CASE 7. A woman, aged 22 years, entered the hospital on September 6, 1944, with a simple comminuted fracture of the tibia and fibula. The wound was cleaned. The patient had also suffered several lacerations to the medial side of her leg; these were sutured. The fracture was controlled with pins and plaster. On the 12th postoperative day a second operation consisting of a sliding bone graft of the tibia was performed. Pus was found in the wound during the operation and culture of this grew Staphylococcus aureus and beta hemolytic Streptococcus. The wound broke down, because of tension and infection, on the 12th postoperative day. Systemic penicillin was given for 18 days postoperatively, and local penicillin ointment therapy continued in the wound for 40 days. A secondary closure was then attempted, but it failed because of tension in the wound. Another 20 day period of local penicillin therapy was followed by a successful secondary closure, at which time relaxing incisions were covered with intermediate thickness skin grafts. At the time of the last closure, the graft was viable, well vascularized, and there was firm union at the fracture site. Following this secondary closure, 100,000 units of penicillin were given intramuscularly for 11 days. The patient was discharged in a cast without weight bearing, 2 weeks after operation. The wounds have remained healed, and there is firm union at the fracture site.

CASE 8. A man, aged 70 years, entered the hospital with an infected compound fracture of the upper tibia and fibula with nonunion, of 15 months' duration. He entered the hospital again suffering from a cellulitis of the leg. Bacterial cultures grew beta hemolytic streptococci, hemolytic Staphylococcus aureus, and gram-positive aerobic sporeforming bacilli. The wound at the site of the compound fracture had been closed since July 29, 1944. No preoperative penicillin was given. Operation was performed on August 7, 1944, and consisted of removal of sinuses, scar, and nonviable bone, followed by insertion of a free iliac bone graft, with metal plate fixation at the fracture site. The wound was closed. Penicillin therapy was begun on the day of operation, and 100,000 units were given daily for 51 days postoperatively. There was a slight sterile serous drainage from the wound for a few days, but it healed completely and promptly. On November 14, 1944, the patient was discharged in a plaster cast. Subsequent clinical and x-ray examinations have revealed firm union of the fracture, and the wound has remained healed.

SUMMARY

Eight patients have been studied in which free bone grafts have been implanted successfully in infected defects in bones in conjunction with penicillin treatment. Seven of these patients had infected fractures of large bones of the lower extremity with nonunion, and one had a contaminated defect resulting from an extensive resection of bone following removal of a secondarily infected tuberculous knee joint. The pathogenic bacteria cultured from the wounds of these patients were hemolytic Staphylococcus aureus in

4 cases, beta hemolytic streptococcus and hemolytic Staphylococcus aureus 2 cases, Escherichia coli and hemolytic Staphylococcus aureus 1 case, and Streptococcus viridans and hemolytic Staphylococcus albus 1 case. Systemic penicillin was given intramuscularly at 3 hour intervals before operations in 5 of the cases, and after operations in all of the cases. The dosage varied from 100,000 to 200,000 units per day. Prolonged treatment extending over many weeks was necessary. The total amount of penicillin used in each of these cases varied from 3 to 8 million units.

The free bone grafting operations consisted of insertion of iliac grafts and metal plates, 4 cases; sliding bone graft and metal plates, 1 case; iliac grafts without metal fixation, 2 cases; and sliding bone graft without metal plating, 1 case. The operative wounds were closed completely in 7 cases and in 1 case the wound was closed around a small soft rubber tube through which supplementary treatment with local penicillin was given. The most recent bone grafting operation was done 3 months ago and this wound has not yet been inspected, but there are no signs of infection and the patient has left the hospital with plaster fixation. Immediate primary healing has resulted in 4 cases; however, in 1 of these cases an adjacent sinus tract reopened following the operation and drained temporarily, and another patient returned for treatment of an infection that developed 6 months after operation. Two wounds developed necrosis and low grade infection resulting from tension at the site of closure, and these have required secondary closure and skin grafting procedures. One wound became infected and required drainage, but the patient was receiving inadequate doses of penicillin at the time.

At present the wounds of 6 of the 7 patients with grafting operations for infected nonunited fractures are healed completely, and 1 (which became infected 6 months after operation) is under treatment. By x-ray examination the bone grafts in all of these cases appear to be viable and in proper position, but 1 graft in a defect of the tibia fractured 4 months after operation and required a supplementary (fibular transplant) procedure. None of the grafts has sequestrated, extruded, or been absorbed. Four patients have firm union of the fracture sites with metal plates still in position, and 2 have firm union without metal plates. One patient has not yet had the original plaster dressing removed, and the remaining patient is the one in which fibular transplant was required because the graft in the tibial defect fractured 4 months after the bone grafting operation.

Even though it has been possible under penicillin therapy to accomplish free bone grafting directly into the infected bone defects successfully in these cases, it is probably more desirable in most instances to attempt to obtain healing preliminary to the grafting procedure by penicillin therapy and, if necessary, operations for removal of sinus tracts, infected granulations, scar, and nonviable bone. The bone grafting may then be accomplished at a later operation in a relatively cleaner field. Adequate dosage with penicillin is a useful adjunct in all such cases in which bone grafting and other operations are done in areas in which there are bone defects infected with penicillin-susceptible organisms.

THE STRUCTURE OF THE CALCANEAL TENDON (OF ACHILLES) IN RELATION TO ORTHOPEDIC SURGERY

With Additional Observations on the Plantaris Muscle

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With Surgical Commentary by EMIL D. W. HAUSER, M.D., F.A.C.S.

IN connection with surgical procedures designed to lengthen the calcaneal tendon, a knowledge of the constituents of the tendon is of fundamental importance. The manner in which the several contributing divisions of the entire tendon terminate—on the os calcis directly, or as elements without direct insertion into bone—determines the point and direction at which partial transection should be carried out; the local breadth of each band is equally important, because upon this dimension depends the width of the incision necessary to allow the required degree of "slipping."

MATERIAL AND METHODS

In the present study observations were made upon one hundred specimens of calcaneal tendon, 83 of them in adult cadavers and 17 in adult individuals studied immediately postmortem. From two selected specimens detailed drawings were prepared, of posterior and anterior aspects (Figs. 1 and 2). Specimen A (Fig. 1, a to c) was dissected in such a way that the fascicular structure of the tendon was emphasized; specimen B (Fig. 2, a to c) illustrates particularly the two major and the accessory components of the common tendon of insertion. The data on relationship between the gastrocnemius and soleus components of the calcaneal tendon were shown graphically (Figs. 3 and 4).

Observations on the plantaris muscle were made on 50 specimens, additive to the group of 150 previously reported from this laboratory.[1]

OBSERVATIONS AND DISCUSSION

A. Anatomical Features

1. General Description. The superficial group of posterior crural muscles is made of three muscles, the gastrocnemius, soleus, and plantaris. As an introduction to the authors' observations their regular anatomical features may be reviewed.[2]

a. Gastrocnemius. The ovoid heads of the gastrocnemius, which are structurally similar, take origin from facets above the femoral condyles by aponeurotic bands marginally placed on each head. These bands descend about two thirds of the way down the muscle. The fiber-bundles of the muscle pass obliquely from the supracondylar areas of origin and from the deep surface of the aponeurosis on each side to the tendon of insertion. This tendon begins as a septum between the two heads, and as a lamina on the deep surface of each head. The septum and laminae soon fuse with the broad aponeurosis which covers the dorsal surface of the underlying soleus muscle. The attachment of fiber-bundles continues to about the middle of the back of the leg. The medial head is the broader and thicker of the two, and it extends farther distalward than the lateral head.

b. Soleus. The heads of origin of the soleus take origin from the following: the dorsum of the proximal extremity of the fibula and the upper third of the posterior surface of the latter's shaft; the intermuscular septum between the soleus and the peroneus longus and the transverse septum over the distal margin of the popliteus muscle; the popliteal line and the middle third of the medial border of the tibia. Structurally, the fibular and tibial heads arise as broad aponeuroses which unite proximally on the deep surface of the muscle in such a way as to form a fibrous arch over the posterior tibial vessels and the tibial nerve. Continuing distally these aponeuroses diverge and grow narrow, but the fibular element is continued on the lateral side and the tibial aponeurosis on the medial side of the muscle as far as the distal quarter of the leg. The main por-

Contribution from the Department of Anatomy (No. 451) and the Department of Surgery, Northwestern University Medical School.

[1] Daseler, E. H., and Anson, B. J. The plantaris muscle. J. Bone Surg., 1943, 25: 822-827.

[2] Bardeen, C. R., in Morris' *Human Anatomy* (9th ed., p. 550).

tion of the belly of the muscle is formed by fiber-bundles which arise from the posterior surface of each of these aponeuroses; descending in an oblique course the fleshy part is inserted, in bipenniform manner, into the deep surface of the calcaneal tendon. This tendon begins as a broad aponeurosis which covers the greater part of the posterior surface of the muscle; its fibers gradually converge to form a heavy fibrous band which is inserted into the calcaneus. The fibers of the tendon are described as taking a slightly spiral course, those on the posterior surface passing from the medial margin toward the lateral surface of the calcaneus, while those on the anterior surface course in the reverse direction. The attachment of the fiber-bundles to the calcaneal tendon continues to within a short distance of the heel. A few of them arise directly from the fibula and from the posterior intermuscular septum. On the deep surface of the belly of the muscle there is an accessory fasciculus which is formed by fiber-bundles that spring on each side from the anterior surface of the aponeuroses of origin of the muscle and have a bipenniform insertion on each side of a thin, oblique tendinous lamina which inferiorly becomes united to the deep surface of the tendon of Achilles.

c. Plantaris. The plantaris arises in close association with the lateral head of the gastrocnemius. The fiber-bundles give rise to a flat, short, fusiform belly, and are united to a narrow tendon which extends along the medial edge of the tendon of Achilles toward the dorsum of the calcaneus, where it terminates in any one of several ways (see hereinafter).

2. Variations. There is considerable variation in the extent of the separation of the different parts of the triceps surae. The tendinous portions of the gastrocnemius and soleus may be separate almost as far downward as the heel. Either or both heads of the gastrocnemius or the soleus may be doubled. A slip from the biceps or semimembranosus of the thigh, or from the linea aspera, or from the floor of the popliteal space may join the triceps to produce a quadriceps surae muscle. On the other hand, one of the heads of the gastrocnemius or the tibial head of the soleus may be missing. A supernumerary fasciculus may extend from the deep surface of the soleus to the calcaneus. The plantaris is exceedingly variable in origin, structure, and insertion. The origin may be from the capsule of the knee-joint, the fascia of the leg, or from the tibia. None of the variations, recorded above, appeared in the present authors' series of specimens. Its tendon may terminate at almost any part of its course in neighboring structures. It may be represented by a fibrous band. It is absent in about 7.05 per cent of cases (Daseler and Anson).

The above description of the fleshy portions of the muscles was confirmed by the authors, but more particular attention was focused on the calcaneal tendon, as made up of the tendinous portions of the gastrocnemius and soleus muscles. Most frequently the plantaris tendon is not incorporated in the calcaneal tendon; however, from the surgical aspect it must always be considered as a part of the calcaneal tendon. The tendon as a whole rotates toward the lateral side, as seen from the posterior surface (hence clockwise in the right tendon and counterclockwise in the left).

The gastrocnemius component of the calcaneal tendon begins as a broad aponeurosis at the lower margin of the muscle bellies of the two heads of the gastrocnemius muscle (Figs. 1, a and 2, a). Its fibers converge as they descend toward the insertion on the calcaneus; they rotate at the same time toward the lateral side of the soleus component. At the insertion, the gastrocnemius component not only makes up the lateral side of the posterior surface, but a portion has rotated to attain the lateral aspect of the anterior surface (Figs. 1, b and 2, c).

The soleus component is thicker than that derived from the gastrocnemius. A broad band of fibers begins high on the posterior surface of the soleus muscle and comes into apposition with the aponeurotic band of the gastrocnemius to which it is rather firmly fixed by fascial fibers. This broad band of fibers runs directly over the posterior surface of the soleus, receiving more tendinous components as it proceeds downward (Figs. 1, b and 2, c); it inserts into the medial portion of the tendon. The tendinous portion, as seen from the anterior surface, usually begins as a single band, high up in the muscular portion where it may be concealed by muscle fascicles (Fig. 1, c). This component increases gradually in size as it descends, and courses obliquely medialward (Figs. 1, b and 2, c). Portions of this anterior group of fibers appear on the posterior surface of the insertion of the tendon as a whole (making up the medial segment) (Figs. 1, a, 2, a and 2, b).

It is regularly stated that almost complete separation may be made between the components (gastrocnemius and soleus) of the calcaneal tendon. Actually, the separation cannot be made absolutely complete, since there is some exchange of smaller bands of fibers between the two[1] (Fig. 1, c). In the experience of the present authors,

[1]Torn fibers in Fig. 1, c are of this type, are shown after separation of the components of the tendon by blunt dissection.

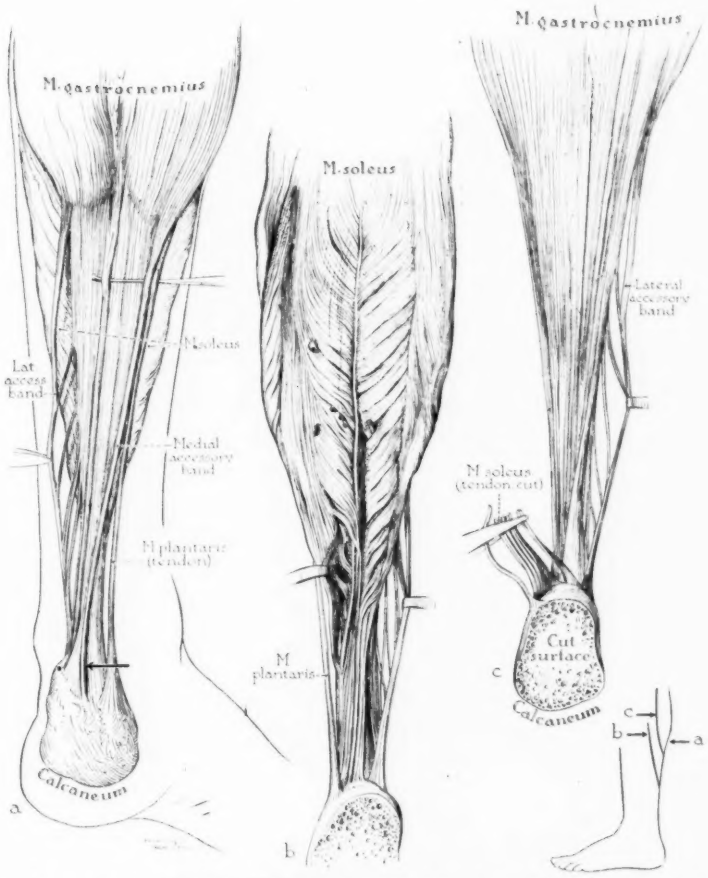


Fig. 1, a to c. Calcaneal tendon, left leg, specimen A (type II). a, Posterior view of calcaneal tendon, with soleus muscle visible beyond margins of tendon and of gastrocnemius muscle. Fibers to reader's left of point of arrow belong to gastrocnemius, those to right are constituents of soleus component of calcaneal tendon. Lateral accessory band of tendon has been retracted by forceps, intermediate and medial bands lifted by probe. Plantaris tendon (of type III) in natural position. b, Anterior view of soleus muscle and calcaneal tendon; os calcis coronally sectioned in front of tendinous attachments. Modified bipenniform character of the soleus is shown, as well as the several bands which emerge from it. c, Anterior view of gastrocnemius part of calcaneal tendon, exposed by removal of soleus part (cut ends of latter held by forceps). Inset records level and direction of view in each figure.

number and strength of fibers exchanged vary greatly; sometimes these fibers are numerous and strong enough to render complete segregation virtually impossible.

For purposes of clear description, representative fibers must be discussed separately in order to account for the several constituents of the tendon. The most lateral band (lateral accessory fasciculus) of the gastrocnemius (Fig. 1, a) rotates to insert on the anterolateral surface of the tendon. This band in the second specimen (Fig. 2, a and c) appears to arise from the posterior aspect of the soleus, and throughout the first half of its course is overlapped posteriorly by, and adherent to, the soleus fibers. About 1 centimeter from its origin it becomes incorporated into the gastrocnemius

tendon from which, however, it is separable by blunt dissection. The fasciculus courses along the lateral surface of the tendon to within 12 centimeters of its insertion, where it rotates to the anterior surface of the calcaneal tendon to fan out and occupy the lateral two thirds of the anterior surface at its calcaneal insertion. An intermediate band (Fig. 1, a), located between the two heads of the gastrocnemius, rotates to insert along the lateral margin. This band is not demonstrable in the second specimen. The most medial band (Fig. 1, a), rotates to insert at the approximate middle of the calcaneal tendon, leaving a considerable portion of the soleus exposed on the posterior surface. Here also, in the second specimen, this band appears to arise from the soleus aponeurosis; however, it soon becomes an integral part of the gastrocnemius tendon with practically no rotation of its fibers (Fig. 2, b). As a consequence, only a small portion of the soleus tendon is visible from the posterior aspect (Fig. 2, a and b). The medial fibers of the gastrocnemius component follow an almost parallel course. This band cannot be separated from the remainder of the gastrocnemius tendon as is possible in the case of the lateral band.

Examination of the deep (or anterior) surface of the tendon reveals the degree of rotation of the soleus component (Fig. 2, c), as well as the insertion of the most laterally situated band of the gastrocnemius portion (Figs. 1, b, 1, c and 2, c). The muscle fibers of the soleus extend farther distalward on the lateral side of the tendon and contribute fibers to the tendon to a point 7 centimeters from the insertion.

A thin fibrous sheath envelops the calcaneal tendon; on the deep, or anterior, aspect, the tissue contains a considerable amount of fat. This sheath is adherent to the fibula except for the distal 10 centimeters; from it originates many of the fibers of the soleus muscle. An even thinner lamina, containing almost no fat, separates the muscular portions of the gastrocnemius and soleus and contains the intervening plantaris tendon.

It is clear then, that the components of the calcaneal tendon vary considerably in size, relationship, and rotation. The length of the gastrocnemius component is the longer, varying from 26 to 11 centimeters in length, in contrast to the shorter soleus component which varies from 11 to 3 centimeters in length. The width of the tendon as a whole varies from 2.5 to 1.2 centimeters at insertion.

Rotation is such that, in the specimens examined, the gastrocnemius covers almost entire posterior aspect in some and in others the entire anterior aspect of the soleus portions (Fig. 3). Some rotation invariably occurs. In order to record degree conveniently, the tendons are arranged in three groups. Group I includes cases of least rotation—in which no more than one third of the tendon posteriorly is contributed to by the soleus, and two thirds by the gastrocnemius. This group comprises 52 per cent of the 100 cases. Group II, including tendons whose rotation is such that approximately one half of the posterior surface is contributed to by each component, represents 35 per cent of the cases. Group III, in which rotation is extreme, so that two thirds of the posterior surface is made up of the soleus and only one third by the gastrocnemius, comprises 13 per cent of the cases. Rotation begins approximately 12 to 15 centimeters from the insertion, or about the level at which the soleus begins to contribute fibers to the tendon. Minimal rotation seems to be associated with lengthy fusion; since rotation occurs only in the "free" portion of the tendon, fusion of the gastrocnemius with a soleus muscle of extensive origin occasions an arrangement which allows the combined tendon to twist only in the distal half of the leg. Progressing slowly at first, the rotation can then become more marked in the lower 2 to 5 centimeters.

In a depression which crosses the posterior surface of the soleus muscle at about the junction of the medial and middle thirds, is lodged the slender plantaris tendon. It remains between the two components of the calcaneal tendon to a point 12 centimeters proximal to its insertion; having attained the medial aspect, it retains that relationship to its insertion (Figs. 1, a, 2, a and c).

When present, the plantaris tendon always occupies a position on the medial surface of the tendon, and varies only in its manner of insertion.[1] In most instances the tendon of the plantaris is found to terminate in a fan-shaped aponeurotic expansion, related to the medial border of the distal extremity of the calcaneal tendon. This and other common arrangements may be conveniently described under the heading of types.

In specimens of type I, representing the commonest mode of insertion of the plantaris tendon (94 of 200 cases, or 47 per cent), the plantaris tendon inserts by a short fan-shaped expansion into the medial extremity of the superior tuberosity for insertion of the calcaneal tendon (Figs. 5, a and 2, a). In some instances the tendon also sends thin slips to the adjacent medial border of the calcaneal tendon. These slips, resembling fascial strands and not true aponeurotic extensions, are

[1]Daseler, E. H., and Anson, B. J. The plantaris muscle. J. Bone Surg., 1943, 25: 822-827.

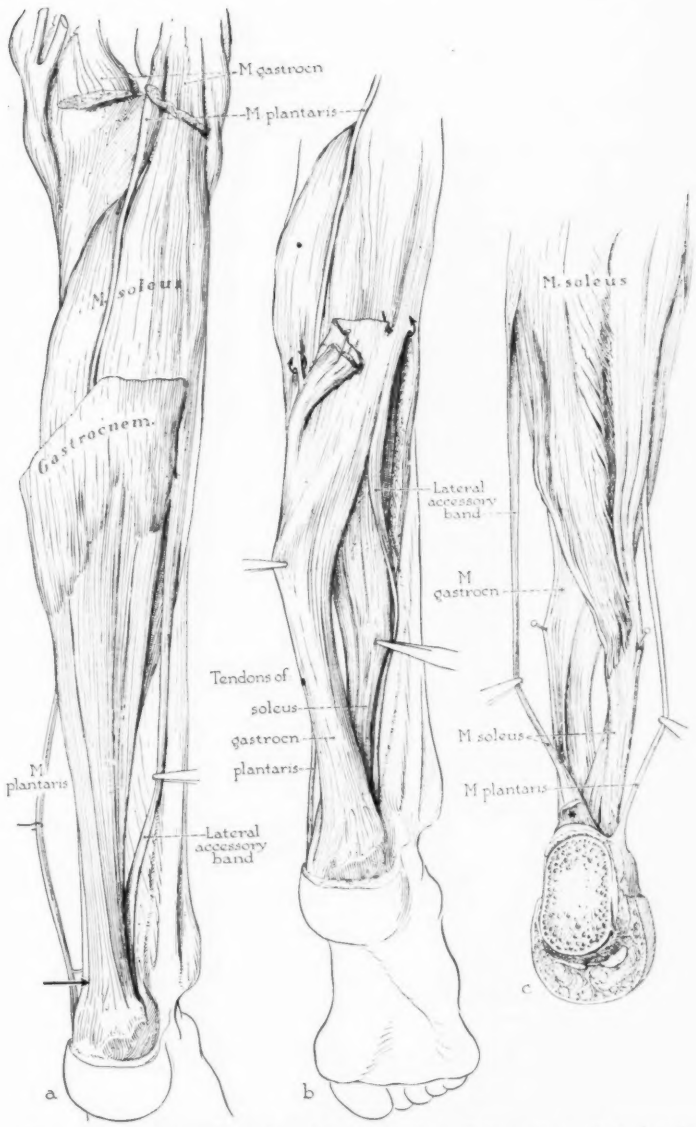


Fig. 2, a to c. Calcaneal tendon, right leg, specimen B (type I). a, Posterior view of calcaneal tendon showing gastrocnemius, soleus, and plantaris muscles; accessory fasciculus retracted to reader's right, plantaris tendon to left. Of calcaneal tendon (type I) small portion to reader's left of point of arrow is soleus component, larger part to right thereof is gastrocnemius division. b, Posterior view of calcaneal tendon showing origin of lateral and medial accessory bands (encircled by curved arrows). c, Anterior view of calcaneal tendon showing lateral accessory band of soleus, major components of calcaneal tendon (drawn apart) and plantaris tendon. Accessory fasciculus attains position on anterolateral aspect of calcaneal tendon, lies deep (anterior) to soleus component of tendon, and terminally forms posterior wall of bursa (at *).

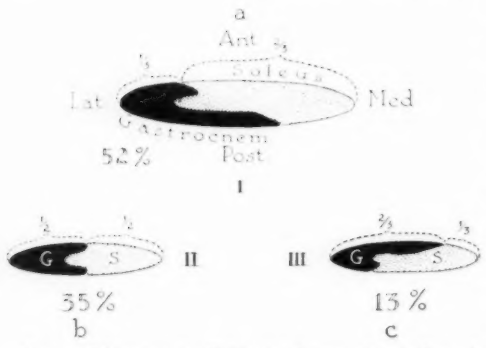


Fig. 3. Diagrams to illustrate degree of rotation of gastrocnemius to soleus portions of calcaneal tendon (as of left extremity), at level of insertion into calcaneus. Occurrence in percentage (of 100 specimens) is indicated for each.

readily removed from the tendon proper. In type II, second in the order of frequency (73 specimens, 36.5 per cent), the plantaris tendon inserts into the calcaneus, 0.5 to 2.5 centimeters anterior to the adjacent margin of the calcaneal tendon (Fig. 5, b); the long axis of the tendon is usually at an angle with, not parallel to, the long axis of the foot itself. The insertion supports the anterior wall of the bursa of the calcaneal tendon (Fig. 5, b, at cross). When large, the tendon frequently radiates in fan-shaped manner to the laciniate ligament and the fascia overlying the medial aspect of the calcaneum (Fig. 5, e); tendinous insertions are frequently quite expansive (Fig. 5, e), and often involve the fascial and ligamentous structures on the superior and medial surfaces of the foot. In type III (25 specimens, 12.5 per cent) the tendon is usually broad at the insertion; but, whether of large or medium size, it invests the dorsal and medial surfaces of the terminal portion of the adjacent calcaneal tendon (Figs. 1, a and 5, c). In specimens belonging to type IV (8 cases, 4 per cent) the plantaris tendon inserts chiefly into the medial border of the calcaneal tendon from 1 to 16 centimeters above the insertion of the latter into the calcaneus; occasionally, however, a lowermost slip may reach the bone (Fig. 5, d).

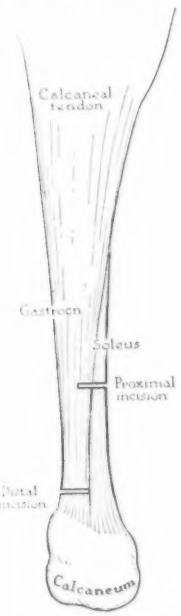


Fig. 4. Diagram to illustrate constitution of calcaneal tendon, showing form of each of its major divisions of gastrocnemius tendon and subjacent position of soleus tendon. Sites of usual incision (tendon, type II) are indicated.

It is clear, then, that the plantaris tendon, in a preponderant percentage of cases, gains a virtually separate insertion into the os calcis. This it may do in any one of three principal ways: by implantation into the os calcis just in front of the calcaneal tendon, the long axis of the line of fixation being parasagittal; by insertion into the bone in such a way that the long axis is almost transverse, beginning, as in the former instance, at the medial margin of the calcaneal tendon; by attachment to the calcaneus medially, or to the calcaneal tendon posteromedially. In the first and second instances, the posterior border of the plantaris tendon is in contact distally with the anterior border of the calcaneal tendon; in the third instance, the lateral, or anterolateral surface is contiguous with the posteromedial surface of the calcaneal tendon. Even in those cases in which the insertion is into the calcaneal tendon, a few fibers may be sent downward for independent attachment to the os calcis.

In the 58 cases of absence of the plantaris in the present authors' series, there are 16 subjects in which agenesis is bilateral, and 26 specimens in which it is unilateral.[1] Thus, in approximately one third of those persons in whom the muscle is wanting, it is bilaterally absent. The muscle is absent on the right side in 23 and on the left side in 35 of the 58 cases. Of the 26 specimens with unilateral absence, 19 are left, while only 7 are

[1] In a series of 881 extremities studied in the Anatomical Laboratory at Northwestern (see Daseler et al.), the plantaris muscle was wanting in 60 cases (7.16 per cent). In sets tabulated from the literature, the percentage absence is 7.05 (187 in 2650).

right. When the muscle and tendon are poorly developed on one side, they are usually equally weak on the opposite side.

B. Surgical Applications

The earliest orthopedic operation recorded is that of lengthening the Achilles tendon. It has become one of the commonest orthopedic procedures. Originally lengthening was accomplished by complete division, following which the gap was filled in by growth of the tendon. Many procedures were later devised. The usual procedure now is the open operation (Z-type tenoplastic) (see Fig. 4). Lengthening can also be accomplished by the subcutaneous method, but in carrying this out many difficulties have been encountered. Irrespective of what method was employed, in certain cases the portions of the divided tendons did not slide as readily as desired; whether the division was taken two thirds anteriorly and two thirds posteriorly, or two thirds medially and two thirds laterally, the results were similarly unsatisfactory.

In the usual open Z-type tenoplastic, the tendon is divided proximally in the medial half and distally in the lateral half, the incisions then connected by a longitudinal cut. After the proper amount of lengthening has been obtained, the tendons are sutured. This has the disadvantages, first, that scar tissue may render the tendon adherent to the skin and underlying structures, and second, that, with a complete division of the tendon, there is no way of controlling the amount of lengthening by "feel." This is important in cases of spastic paralysis since the object is to obtain a better muscle balance between the opposing groups, by weakening the stronger group. The amount of weakening to be obtained can best be judged if the lengthening is taken against the resistance of the tendon. With the subcutaneous method, and through sliding by of the fibers of the tendon (without a complete division), the introduction of sutures is not necessary and consequently there is less reaction. Additionally, the danger of infection is further reduced.

In the anatomical descriptions presented the authors show that in some cases the tendon fibers run practically straight and parallel (Fig. 2, a), while in others there is a complete rotation (Figs. 2, c and 3, c); all intermediate stages can be found, between these extremes (Fig. 1, a). In addition to difficulties occasioned by variation in the course of the fibers, others arise out of failure to divide the plantaris.

The objective of the surgeon is to divide one half of the fibers of the tendon of Achilles proximally and the other half distally, and at the same time divide the plantaris tendon with the simplest possible procedure.

Rotation of the calcaneal tendon was first brought to our attention by White,[1] who describes it as a constant occurrence which is established during embryological development. Because of this concept he advises sectioning the anterior two thirds of the tendon distally and the medial two thirds proximally. As demonstrated by the current observations, the rotation is variable, not constant. In carrying out White's method it is necessary in certain instances to make a third incision, dividing some gastrocnemius fibers laterally at the same level as the anterior section, in order to permit the severed fibers of the tendon to slide by. This is easily understood when it is remembered that a certain percentage of tendons of type I undergo very slight rotation (Figs. 2, a and 3, a). Therefore, enough of the gastrocnemius fibers remain undivided to require a third section before proper lengthening can be obtained. The method described by White is an excellent procedure in most cases, but unsuccessful in a sufficient number of those cases with slight rotation so that this study was thought advisable. In addition, the technique is difficult to perform subcutaneously, without visualization, because the distal end of the tendon lies deep, making the anterior half accessible only with difficulty. For this reason most surgeons expose the tendon with a longitudinal incision.

To overcome the difficulty just described the authors advise the following procedure. A proximal section is made to divide the posterior two thirds of the tendon (the gastrocnemius portion) (Fig. 6, b), and a distal one to separate the medial two thirds (the soleus fibers, including the plantaris tendon) (Fig. 6, c). In this way all of the fibers are severed either at the proximal or distal level, except in those cases in which there is virtually no rotation of the tendon. In such instances there are a few lateral fibers of the soleus left undivided at the level of the proximal incision. Since these fibers are mainly muscular, due to the extensive distalward site of origin (Fig. 2, c), they are readily torn (Fig. 6, d). As a consequence, the tendon is allowed to slide by, and desired lengthening is easily achieved.

The technique consists in a sterile preparation of the skin, and insertion of a thin tenotome (Fig. 7, a), scalpel-like, through the tendon so that two thirds of the tendon lies posterior to the tenotome. The tenotome is inserted so that the

[1]White, J. Warren. Torsion of the Achilles tendon; its surgical significance. Arch. Surg., 1943, 46: 784-787.

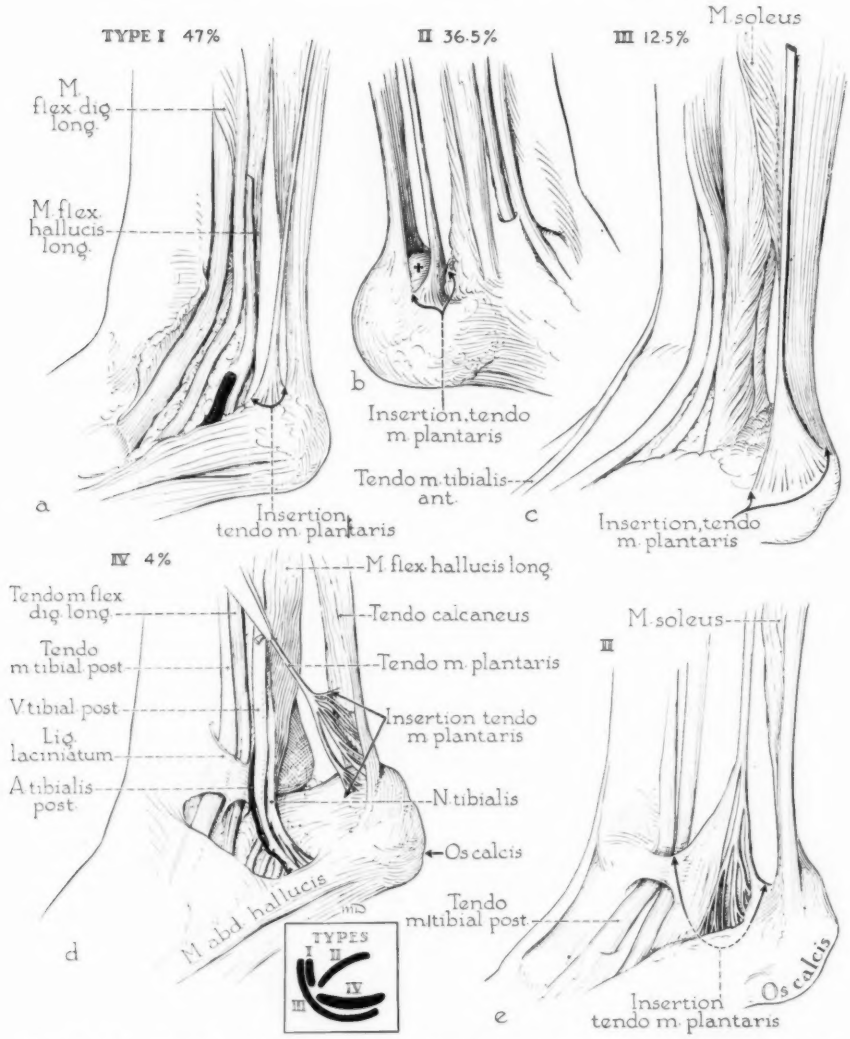


Fig. 5, a to e. Types of tendinous insertion of plantaris muscle (adapted from Daseler and Anson, and augmented); specimen in Figure 5, b is of the left extremity, those in Figures 5, a and c to e are of the right. Bursa in 5, b is indicated by cross. Insert indicates areas of calcaneal insertion of plantaris tendon (types I, II and III) and of combined calcaneal and plantaris tendon (type IV), with areas of insertion numbered to record types. In insert tendon for type IV represented is an unusually long example. For tendon of type II, one of intermediate position is diagrammed; others would lie in front of or behind area indicated.

blade is parallel with the tendon. Next, the blade is turned so that it faces posteriorly, and the tendon is cut through toward the skin. Palpation by the thumb is used as a guide to the position of the blade. The second incision is made distally by means of a curved tenotome (Fig. 7, b). The blade is inserted deep to the medial two thirds of the tendon. The tenotome is then drawn poster

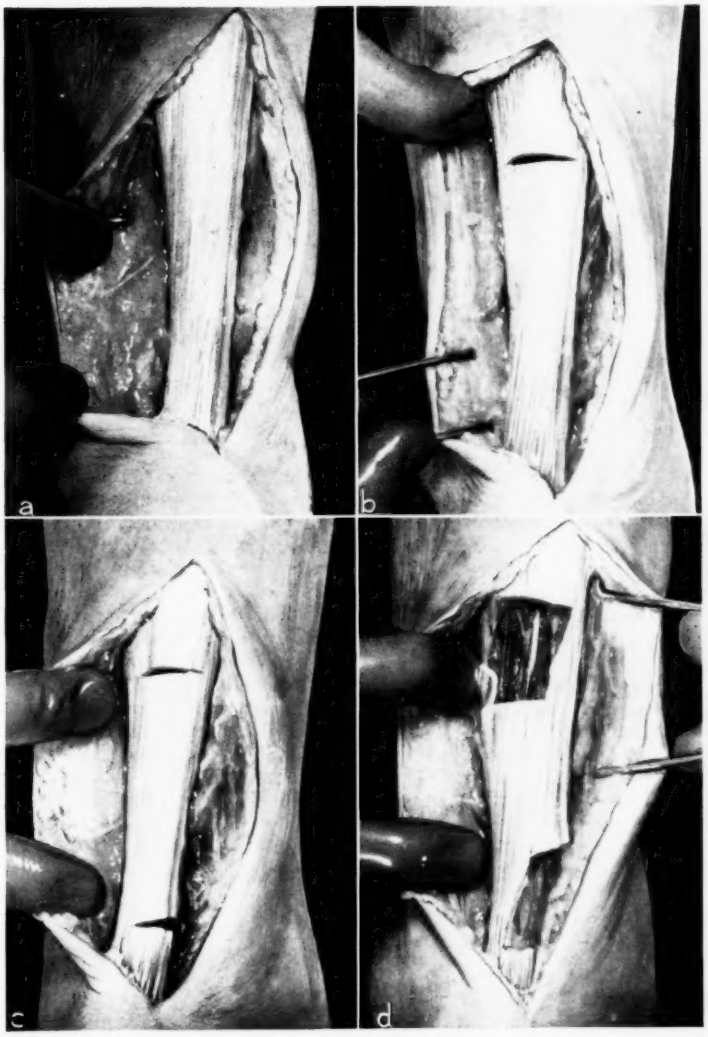


Fig. 6, a to d. Photographs (retouched) of surgical case, illustrating steps in procedure of tendon lengthening. Left leg. a, Calcaneal and plantaris tendons in position; fibers course laterally and counterclockwise. b, Proximal incision, with gastrocnemius and some soleus fibers divided. c, Distal incision dividing plantaris and remainder of soleus fibers. d, After moderate dorsiflexion of foot, showing sliding by of tendon segments and accessory fasciculus of soleus at the center of proximal incision.

iorly and medially to divide the medial two thirds of the tendon. The distance between the two divisions can vary from 1 inch to 4 or 5 inches, depending on the amount of lengthening required. The proximal incision should be made a distance of 3 to 5 inches from the insertion of the tendon into the calcaneus, depending upon the amount of increase desired in the length of the tendon. The distal division of the tendon is always made at least one-half inch above the in-

Fig. 7, a and b. Photograph of tenotomes used. a, above. Used for proximal incision. Blade length 1.3 centimeters. b, Curved tenotome used for distal incision. Blade length 1.0 centimeters.

sertion of the Achilles tendon; in this way the tendon of the plantaris muscle is always included in the second incision. After the tendon has been divided in this manner, little force is required to lengthen the tendon, since the fibers will slide by quite readily. Judgment is required to establish the proper degree of lengthening. In cases of spastic paralysis the resistance present under anesthesia is a factor to be considered. The amount of correction can be measured by the amount of dorsiflexion taken. Palpation of the gaps in the tendon is also serviceable in establishing the degree of lengthening. Postoperatively the extremity is put in a cast to retain the new position and to allow the tendon to heal with retention of its increased length. A little less than the full correction obtained by surgery is to be maintained by the cast, in order to avoid undue strain and to prevent the formation of pressure sores.

In brief, then, the authors recommend the closed technique for lengthening the calcaneal tendon wherever its employment is possible. Basing a judgment upon an extensive anatomical study of cadavers and of postmortem specimens, and after considerable orthopedic experience, the authors feel justified in recommending their modified form of a well known surgical technique.

SUMMARY

In a group of one hundred lower extremities the constitution of the soleus and gastrocnemius tendons and of the combined calcaneal tendon was studied. Typical specimens are illustrated.

Some rotation of the gastrocnemius to the lateral side occurs in every case. The degree of rotation varies from slight (to render the soleus just visible in dorsal view), to extreme (causing the soleus component to be nearly obscured from the ventral surface). Cases of extreme rotation are far less common than those in which moderate rotation obtains.

Ability to separate the two components likewise varies from a condition in which it can be carried out with ease to one in which segregation is practically impossible. The width and length of the two components likewise vary to a marked degree.

The plantaris muscle and its tendon are subject to considerable variation in both origin and insertion. From an examination of 200 lower extremities, the authors set up four types of tendinous insertion. In a total of 810 consecutive lower extremities examined by the authors, the plantaris muscle is absent in 58 (7.16 per cent). In one third of the specimens in which the muscle is missing, the absence is bilateral.

Various types of transverse incisions were made on exposed tendons and ability to cause "slipping" by moderate dorsiflexion of the foot noted. From these observations, subsequently established clinically, it is concluded that if the posterior two thirds of the tendon be sectioned proximally and the medial two thirds distally, the desired degree of lengthening can be produced. It is also concluded that, by subcutaneous tenotomy rather than a more extensive tenoplastic procedure, it is possible for wholly satisfactory results to be obtained.

FOREIGN BODIES IN, AND IN RELATION TO, THE THORACIC BLOOD VESSELS AND HEART

I. Techniques for Approaching and Removing Foreign Bodies from the Chambers of the Heart

DWIGHT E. HARKEN, M.D., Lieutenant Colonel, M.C., A.U.S., Brookline, Massachusetts

THE purpose of this short discussion is to outline briefly a few aspects of the problem of foreign bodies in relation to the thoracic blood vessels and heart. Principal attention will be given: first, to the location of the missiles, second, to some reasons for the surgical removal of such bodies, and third, to the technique of approaching and removing fragments from the chambers of the heart. The necessity for brevity will dictate certain dogmatism and even the use of unsupported statements. Further clarification and support are to be presented (1, 2).

During the past 10 months with the thoracic unit of the 160th General Hospital 78 missiles were removed from within or in relation to the great vessels, at least 3 of which were embolic. During the same period 56 foreign bodies in, or in relation to, the heart have been removed, 13 of which were in the chambers of the heart. The great vessel series of 78 cases and the cardiac group of 56 cases, represent a total of 134 patients and 139 operations. There have been no deaths. A more precise breakdown in the distribution of these missiles is as follows: pericardial, 26; involving pericardium but principally pulmonary, 17; intracardiac, 13; on great vessels (and in walls), 35; intravascular (3 embolic), 7; on great vessels but principally pulmonary, 17; mediastinal but not directly on great vessels, 19, a total of 134, with no deaths.

The first diagram (Fig. 1) is a scale drawing of the heart and great vessels presenting the approximate size and location of a few of the foreign bodies first removed in the Unit. The gray shading represents a position impinging on the indicated structure, cross-hatching signifies an embolus and black indicates removal of foreign body from within the structure designated.

A current diagram (Fig. 2) has been prepared but in representing 129 missiles it has been necessary to use point localization only. The same key to location is used in the margin, gray for foreign bodies impinging on the structure, cross-hatching for the embolic missiles and solid black for those lying within the structure outlined.

About all that such a gross method of localization conveys, is that the foreign bodies occupied a variety of positions, diffusely distributed about the mediastinum but that only one was found to lie in the left ventricle and none within the lumen of the thoracic aorta. It is, therefore, assumed that the direct entrance of foreign bodies of surgical size into either of these structures is rarely sur-

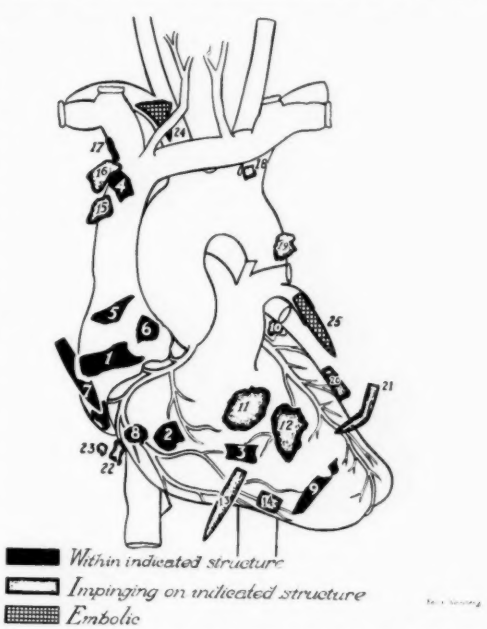


Fig. 1. A scale drawing of some of the first missiles removed in this clinic. Gray shading, impinging position; cross hatching, an embolus; black, within structure designated.

From the 160th General Hospital.
Presented at meeting of the Association of Surgeons of Great Britain and Ireland, May 2, 1945.

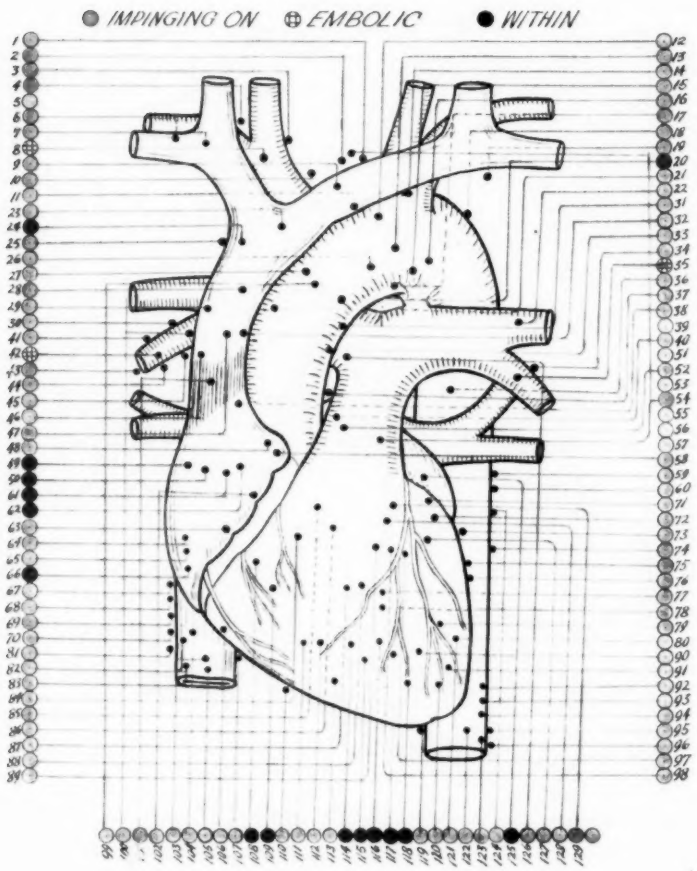


Fig. 2. Gross localization of foreign bodies presented in this discussion. Gray, impinging; cross hatching, embolic missiles; black within structure.

vived. It is further suggested that fragments small enough to enter the left ventricle as migrating missiles are swept along by the high systemic pressure in contrast to those arriving at the right ventricle.

FOREIGN BODIES IN OR ON GREAT VESSELS

The danger of erosion and suppuration attending large retained missiles in relation to thoracic blood vessels is real. Three deaths from massive hemorrhage due to erosion have come to our attention. Furthermore, approximately 15 per cent of the thoracic vessel foreign bodies in our series have been associated with abscess formation, just over 30 per cent were associated with other foreign material such as cloth or bone and 67 per cent showed pathogenic bacteria on culture. It is therefore, our policy to remove all foreign bodies measuring one or more centimeters in two dimensions, at times smaller missiles are taken out. The technical aspects of finding such fragments at operation are insignificant. We have failed in only one instance and that, the third case in this clinic. The fact that there have been no deaths supports our contention that removal is safer than retention.

In passing, attention is called to the three foreign bodies that have been established as embolic

one was from the liver to the left pulmonary artery, another traveled from the heart to lodge in the innominate artery, and the third shifted from the left to the right pulmonary artery. All of these were removed without incident and with restoration of vascular continuity. These will be reported in detail separately (1).

FOREIGN BODIES IN OR ON THE HEART

Of the 56 foreign bodies in, or in relation to, the heart 13 have been removed from the chambers of the heart. The locations of the missiles in the chambers of the heart are indicated in the photograph (Fig. 3). Four were in the right auricle, 5 were in the right ventricle, 1 was in the left auricle and 1 was in a small cystic myocardial hernia of the left ventricle.

One fragment listed as within the right auricle lay in the interauricular septum and was associated with systemic embolus producing hemiplegia. Another fragment, described as in the right ventricle, was more evasive than the others (LeR.R. in Fig. 3). At the first operation with the patient in the dorsal decubitus position, the fragment wriggled from the grasping forceps and migrated to the right auricle just over the opening of the inferior vena cava. Three months later at the second cardiotomy the missile, though surgically exposed and visualized fell from the auricle into the right ventricle—the direction of fall being influenced by the patient's left lateral decubitus position. Finally at the patient's request a third cardiotomy was performed and the fragment was trapped in the apex of the right ventricle and successfully removed. The patient is now apparently in robust health. The last operation was recorded in colored moving pictures which demonstrate the firmly healed cardiotomy of the

Fig. 3. Photograph of intracardiac missiles that have been removed.

first operation and an area of damaged wall over the last intracardiac resting place of the migrating missile. This case demonstrates that even migrating foreign bodies can damage the overlying heart wall.

In spite of isolated reports of asymptomatic foreign bodies lodged in the heart, there is also evidence in the medical literature that some do cause death. These reports together with experimental evidence were the early basis for a policy of surgical intervention. It was found that foreign bodies placed inside the hearts of animals were associated with subsequent bacterial endocarditis. With such a background it was elected to remove 13 of 28 intracardiac foreign bodies. *It was felt that certain foreign bodies should be removed:* (1) to prevent embolus of the foreign body or the associated thrombus; (2) to reduce the incidence of

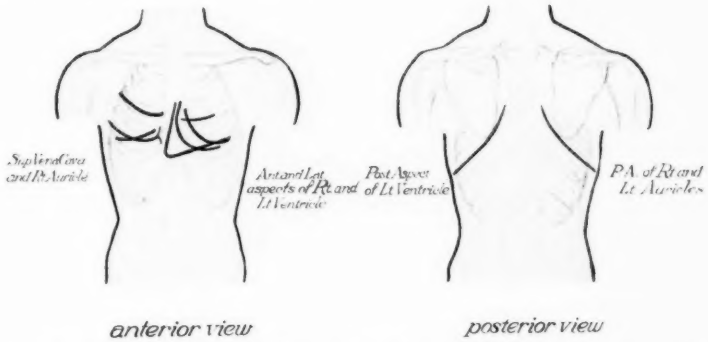

Supl'rior Vena cava and Rt Auricle
Ant and Lat aspects of Rt and Lt Ventricle
Post Aspect of Lt Ventricle
P.A. of Rt and Lt Auricles
anterior view
posterior view

Fig. 4. Some of the incisions, indicating the variety of approaches used to obtain adequate direct exposure.

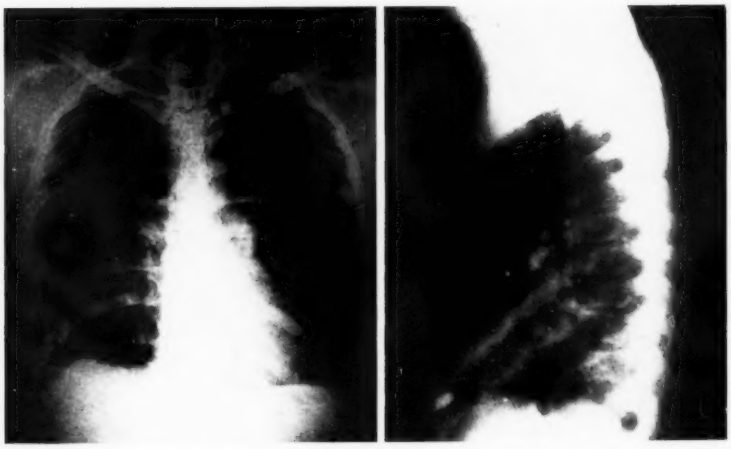


Fig. 5. Anteroposterior and lateral views of a foreign body in the chamber of the right ventricle. The right hemithorax was cleared of an infected hemothorax by decortication before these pictures were taken.

bacterial endocarditis; (3) to avoid recurrent pericardial effusions; and (4) to diminish the danger of myocardial damage with subsequent rupture or myocardial aneurysm.

It is now fair to say that this rationale originally borrowed from the medical literature and partially confirmed by personal animal experimentation, has been clinically established. The evidence cannot be reviewed here, but will be further elaborated in a later publication (2).

Inevitably size and location are factors influencing surgical intervention. Small foreign bodies are probably less hazardous as they may be associated with less myocardial damage, they are

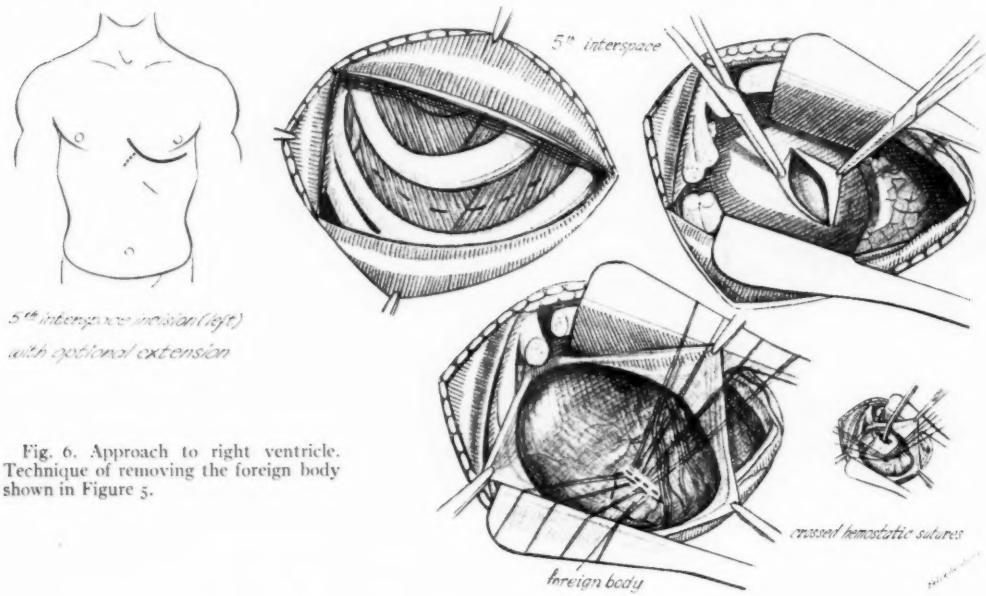


Fig. 6. Approach to right ventricle. Technique of removing the foreign body shown in Figure 5.

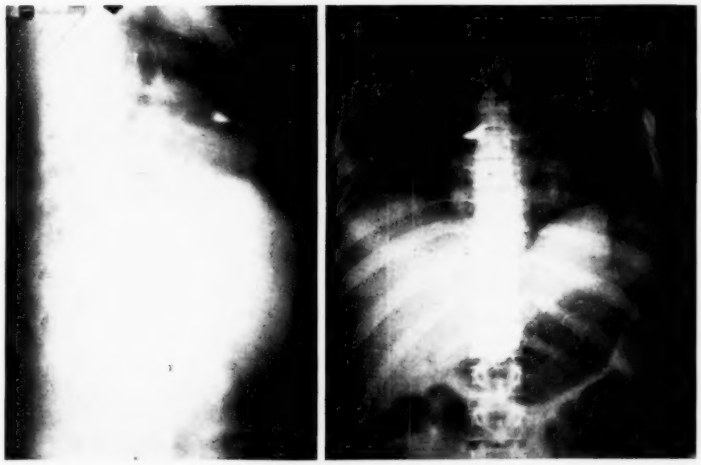


Fig. 7. A missile is shown to lie in the right auricle.

more readily and more firmly encapsulated and, finally, small foreign bodies are technically more difficult to remove. Accordingly in this clinic, the retention of 15 foreign bodies apparently in the heart has been regarded as less hazardous than their surgical removal. In short, Figure 3 illustrates the foreign bodies that we have elected to remove. Size alone dictated removal of some of these, whereas, attending clinical manifestations influenced the decision to intervene in others.

Once the decision to remove a missile from the heart is made, the technical considerations are contingent upon surgical exposure and safe removal at cardiotomy.

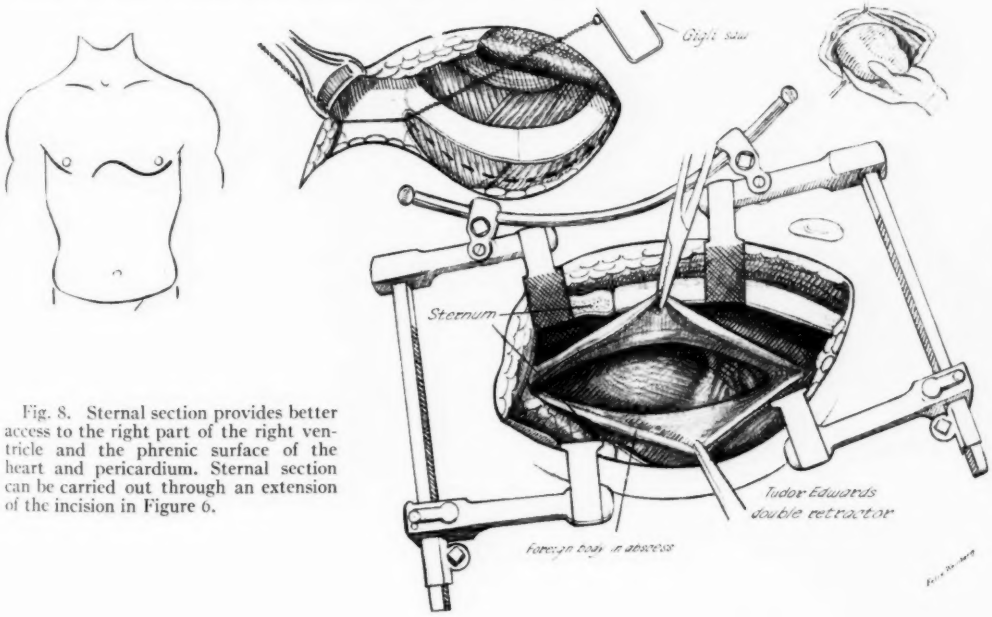
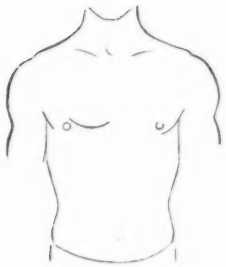


Fig. 8. Sternal section provides better access to the right part of the right ventricle and the phrenic surface of the heart and pericardium. Sternal section can be carried out through an extension of the incision in Figure 6.



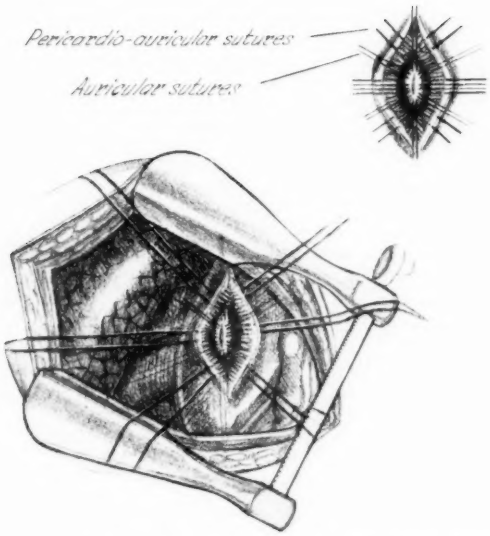


Fig. 9. The technique of approaching and exposing the fragment shown in Figure 7—anterior approach to the right auricle.

SALIENT FEATURES OF CARDIAC EXPOSURE

1. Adequate direct exposure of the involved region. This wide, direct exposure necessitates the use of a variety of approaches (Fig. 4) each one focused on the immediate problem at hand. This means that no standard or set cardiac approach is relied upon. The pleura is routinely opened.

2. Conservation of thoracic cage skeleton. The free division of ribs, cartilage, and the sternum is often essential; but complete reconstruction of an intact chest wall at end of operation must be borne in mind. Nothing is resected, nor discarded.

3. Minimal dislocation of the heart from its position of optimum function. Dislocation, manually or by means of an apical suture is badly tolerated and has caused runs of ventricular extrasystoles, diminished cardiac output, and transitory bundle branch block. Cardiac surgery with minimal dislocation of the heart, indeed, taxes the versatility of approach first emphasized.

4. Maintenance of a moist epicardium in the exposed heart. One per cent novocain solution has been used to keep the epicardium moist. It may have additional advantages.

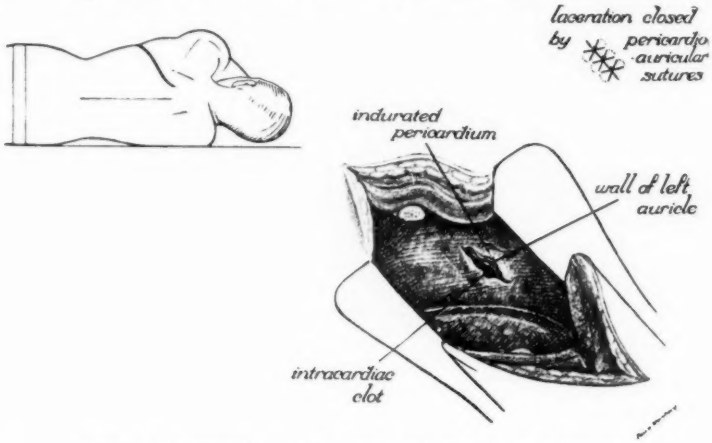


Fig. 10. The approach used to remove a missile from the left auricle.

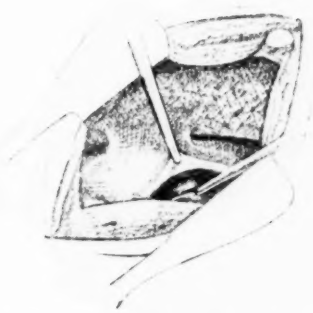


Fig. 11. A posterior approach to the heart is shown. The patient is in the ventral decubitus position.

Bearing in mind these principles of cardiac approach the left part of the right ventricle and the left border of the left ventricle have been exposed through the fifth or fourth intercostal space (Figs. 5 and 6). The pectoralis major muscle is split laterally and divided medially. The intercostal muscles are divided and the internal mammary vessels ligated. The suprajacent cartilage is divided near the sternum and the rib spreader inserted. Additional exposure can be obtained by the optional "T" incision and the division of the sixth and seventh costal cartilages (see Fig. 6). The pericardium and pleura are then opened freely. The foreign body can then be palpated if it is in the right ventricle. Ordinarily we would not open a chamber of the heart to attempt removal of a missile not precisely located by palpation. Immediately over the foreign body a row of sutures is placed on either side of the projected incision. These are the hemostatic guy sutures or the control sutures by which the assistant prevents blood loss in the opened heart between intracardiac maneuvers. Actually we place two rows of control sutures on each side of the incision. The second row is a second line of defense as one of the first row is often pulled out. The missile is stabilized as well as possible with the fingers, a small epicardial incision is made with the

Fig. 12. A foreign body is shown in the interauricular septum and right auricle. The widened mediastinum was found, at operation, to be due to hematoma.

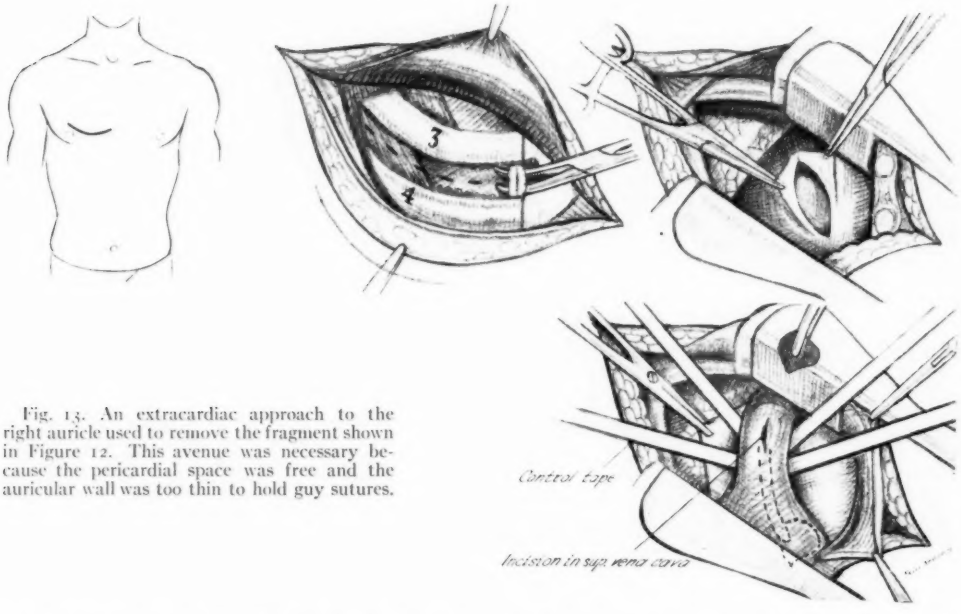


Fig. 13. An extracardiac approach to the right auricle used to remove the fragment shown in Figure 12. This avenue was necessary because the pericardial space was free and the auricular wall was too thin to hold guy sutures.

scalpel and a pointed forceps is thrust through the myocardial wall and spread to make an opening large enough to allow the insertion of a Kocher clamp. The foreign body is then grasped and extracted with the Kocher instrument. During these manipulations, the assistant affects hemostasis by crossing the control sutures. Once the foreign body has been removed, the inner rows of control sutures are tied across the incision. The second line of sutures are then tied over a free pericardial graft. Finally a larger free pericardial graft is placed over the first. No. 00 chromic catgut sutures on atraumatic noncutting needles are used. It is possible that silk would be preferable for use in closing the left ventricle. Postoperative cardiac tamponade is avoided by leaving the lateral angle of the pericardial incision open into the pleural space.

When the region to be approached is farther to the right or on the diaphragmatic surface of the heart, the intercostal incision is combined with transverse sternal section (Fig. 8). Mr. Tudor Edward's double retractor can be adapted for use in this procedure as illustrated. The sternum can be readily reconstituted with wire. When the auricle or the right side of the ventricle is to be approached, the reverse of this incision on the right side of the chest can be used in precisely the same way.

In approaching the right auricle ordinarily the right anterior approach is best, the third, fourth, or even fifth interspace being used, depending on the location of the foreign body. In the operation illustrated in Figures 7 and 9 the third interspace was used with section of the third and fourth costal cartilages near the sternum to gain exposure of the upper portion of the right auricle. In such approaches to the right auricle after the pericardium is opened, control sutures are placed in the auricular wall similar to those in the ventricle. As the auricular myocardium is often too thin to hold the sutures, the pericardium may be included with the auricle in the outer line, if there are existing adhesions as in this case.

A foreign body in the left auricle was approached as indicated in Figure 10. The fusion of the auricle to the pericardium made the intracardiac portion of this operation quite simple. The laceration of the auricle and pericardium was plugged by an infected clot. This patient had had three major and two minor hemorrhages.

A posterior approach exposing the left auricle either on the right or left side has been used to remove intrapericardial missiles but not for an intracardiac operation to date. The patient is placed in the ventral decubitus and the posterior incision provides exposure as illustrated in Figure 11.

In one instance an extremely thin walled auricle was encountered in a completely free pericardial space. The auricle bled when an attempt to place the hemostatic sutures was made and this technique had to be abandoned. Similarly an approach through the auricular appendage was found unsafe. In this instance an extracardiac approach was devised by exposing the superior vena cava (Figs. 12 and 13) control tapes were placed around this vessel, an incision was made as illustrated and a forceps was slipped down the lumen into the auricle. By this maneuver the missile was removed without difficulty.

All of these approaches have been used successfully. Another extracardiac avenue to the heart by way of the pulmonary veins to the left auricle or even left ventricle has appealed to us but no occasion to use it has arisen.

Throughout these operations electrocardiograms have been taken, and these tracings are helpful in determining which manipulations are badly tolerated by the heart. Comments about these findings must be deferred.

Although the electrocardiogram may return to normal within a few hours, the patients who have had *ventricular* cardiotomy are kept in bed for 3 weeks.

SUMMARY AND CONCLUSIONS

1. A series of 78 foreign bodies that have been removed from within, or in relation to, the thoracic great vessels is discussed. Three of these were embolic.

2. A series of 56 foreign bodies that have been removed from within or on the heart is discussed. Thirteen of these were removed from the chambers of the heart.

3. Indications for the removal of certain great vessel and cardiac foreign bodies are discussed.

4. The salient features of cardiac exposure are presented.

5. Various techniques and approaches are outlined for removing foreign bodies from the chambers of the heart.

In conclusion it is again emphasized that the mortality and morbidity rates for retained foreign bodies in and in relation to thoracic blood vessels and the heart have not been completely assessed. However, in our series of 134 patients who have had foreign bodies removed, there have been no deaths and the men are clinically well. We hope that this experience supports our therapeutic policy.

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FRACTURES OF THE UPPER END AND SHAFT OF THE HUMERUS

A Simple Conservative Method of Treatment

LAURENCE JONES, M.D., Beverly Hills, California

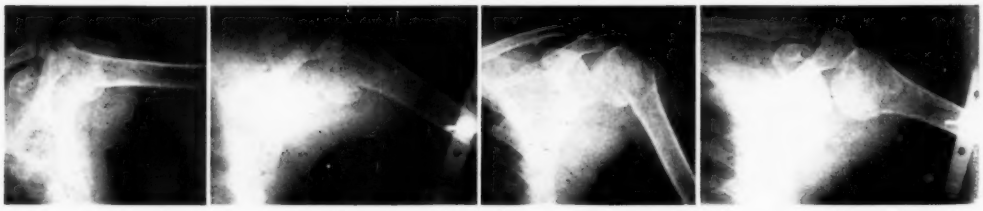
IN October 1942 (1) there was reported, in considerable detail, a reconstructive plastic operation made necessary by a previous resection of the head of the humerus. This operation was indicated when fracture dislocation of the head was present, or when severe comminution made satisfactory reduction impossible.

It was stated that this operation was reserved only for cases in which conservative measures had failed. In actual clinical experience the conservative treatment succeeded in at least 90 per cent of the total number of cases. This conservative method, previously undescribed, varies quite radically from other reported methods of treatment. It has been modified repeatedly over a period of 20 years. Because of a recent change of address, it is impossible at this time, to collect case reports of a rather large series of cases. However, the difficult nature of the illustrative case history should serve to demonstrate the efficacy of this method. It should also be apparent that the method would be applicable to other cases of simpler types. The comparative advantages of this treatment will be discussed briefly.

Mr. D. L. H., aged 66 years, slipped on the sidewalk falling directly on the point of the left shoulder. The arm and forearm were not extended. Immediately thereafter he noticed extreme pain in the left shoulder joint, aggravated by any movement. The patient was removed to the hospital and roentgenograms were made. These showed a badly comminuted fracture of the head, with overriding of the shaft (Fig. 1a). An abduction splint of special design (to be described in considerable detail) with incorporated bracket for skin traction was applied. This bracket was designed to hold two lateral and parallel adhesive skin bands. After 2 days there was little or no improvement in position. Realizing that skeletal traction was necessary, a short Steinmann pin was drilled through the olecranon process of the ulna, and a yoke and different bracket were applied to the abduction splint (Fig. 2a and b). Through this device about 10 pounds of spring traction was applied. The angle of the brace was changed several times until the lower fragment was finally placed in satisfactory alignment with the upper comminuted fragments. All of this was checked by roentgenograms (Fig. 1 b, c, d). Within 1 week a practically complete anatomical reduction had been obtained. Patient became ambulatory and was discharged home.

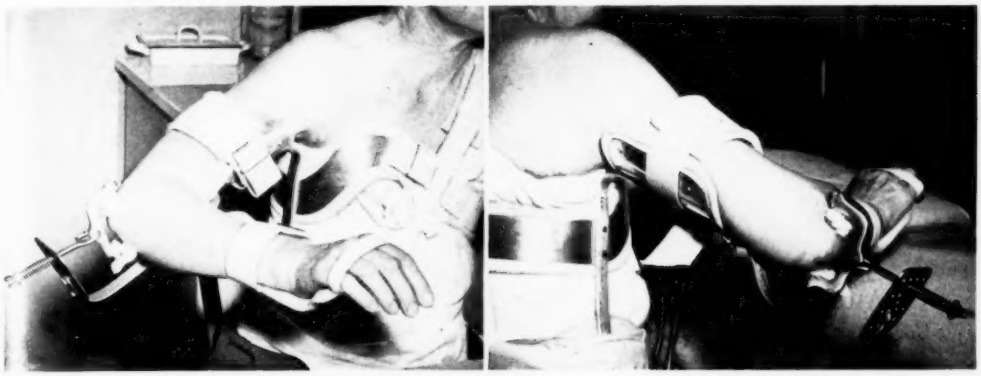
Two weeks after insertion, the Steinmann pin was removed. To prevent angulation and loss of position, the splint itself was not removed until firm bony union could be demonstrated by roentgenograms. This occurred approximately 3 months after date of initial injury. In the interim, patient received physical therapy consisting of inductothermy and massage. No active or passive motion was permitted until firm bony union was demonstrated. Photographs taken 3 years after injury show that patient could carry 30 pounds of sand bags in full abduction (Fig. 3 a). A painless range of motion had been regained, patient's sole disability consisting of inability completely to extend injured arm overhead (Fig. 3 b, c, d).

The abduction splint (Fig. 4) which occupies such a prominent place in this discussion has been modified many times over a period of 20 years. It has become an indispensable addition to the armamentarium of conservative treatment of several conditions. Certain of its features are believed to be original, others were adapted from certain improvements found in other abduction splints. In clinical practice it is used for treatment of fractures of the clavicle. In addition, it has



a b c d

Fig. 1. a, Photograph of roentgenogram illustrating fractures at, and above, the surgical neck with marked comminution of the head and overriding of the shaft. b, c, d Photographs of serial roentgenograms illustrating gradual improvement in position following application of abduction splint.

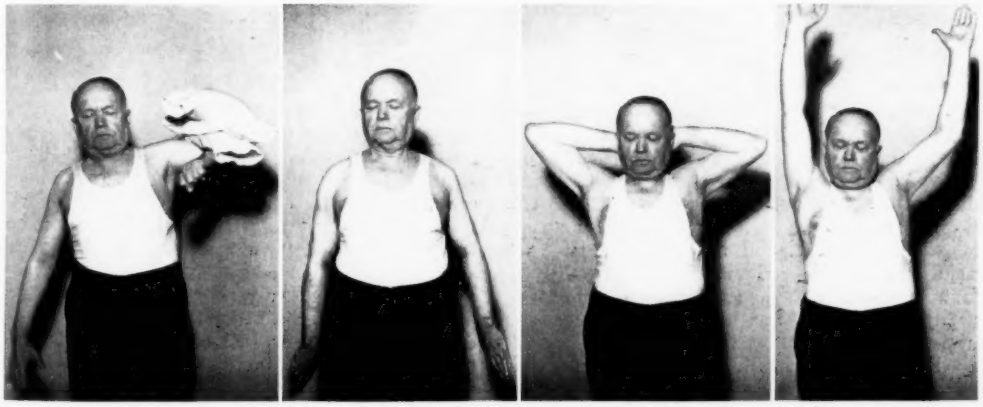


a b

Fig. 2. a, b, Photographs illustrating actual application of skeletal traction in recent patient having a fracture through the surgical neck of the humerus. These two views show ambulant treatment and skeletal traction by Steinmann pin or Kirschner wire. Also improved bracket and yoke with details of spring traction regulated by wing-nut.

been found that immobilization of the shoulder promptly relieves severe pain which accompanies incomplete ruptures of the supraspinatus tendon. These are usually termed subacromial, or subdeltoid bursitis. Compared to other abduction splints it is very light, the frame weighing only slightly more that 2 pounds. This light weight is due to the fact that the frame is made of duralumin, or of thin sheet steel if this is not obtainable. All the various parts can be adjusted to the body contour by simple hand bending. Similarly, the angle of abduction can be adjusted. In treatment of fractures, the bracket in Figure 2a, b is added.

There is no need to describe in detail all of the features of the splint, such as the cock-up forearm splint, the elbow lock, the cupped-up arm rest, and the special design of the pelvic rest, as the accompanying photographs and illustrations do this adequately (Figs. 4a, 4b, 4*d*, 2a, and 2b). However, particular attention should be called to the key strap which starts at the upper bar posteriorly, and attaches to the lower bar anteriorly. This is always the first strap adjusted and has been called the "key strap." Adjustment of this strap assures a snug fit of the brace to the axilla. Also attention is called to the curve in the



a b c d

Fig. 3. Photographs illustrating extent of functional return. a, Photograph illustrating patient carrying 30 pounds of sand bags in full abduction. b, Illustrating complete return of external rotation. c, Illustrating complete return of internal rotation. d, Sole disability is inability to completely elevate arm to the overhead position.

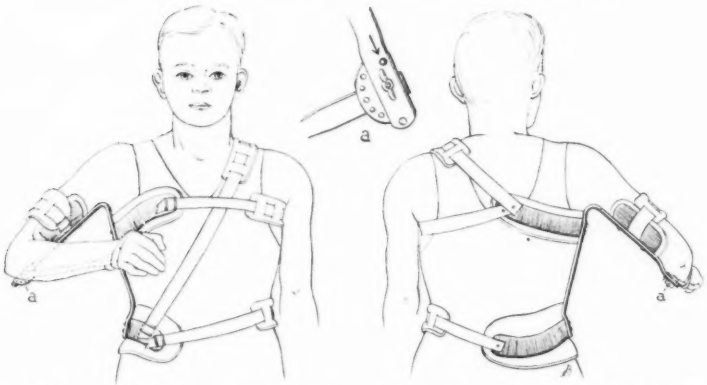


Fig. 4. a, left and, b, right. Anterior and posterior views of abduction splint with special built-in feature. The anterior view illustrates the two bands connected by a vertical connecting bar. When possible, the entire splint is made of duralumin. It weighs a little more than 2 pounds completely equipped and is easily adjusted by simple hand bending. The upper arm band is curved upward anteriorly to avoid pressure on the female breast. The lower body band is designed to fit on the curve of the crest of the ilium. The forearm is curved upward anteriorly under the palm to give a "cock-up" feature. The elbow lock, *a*, is adequately illustrated and capable of fixation or movement as desired. Special attention is called to the "key strap." This is the first strap adjusted and starts at the outer posterior end of the upper arm band and runs to the anterior surface of the lower arm band. The remaining straps pass circularly about the parts. (One central forearm strap is not shown in the illustration.) The frames can be used over and over again with only the felts and straps being changed. The splint can be reversed, for use on opposite side, by a brace shop.

anterior portion of the upper body band. This feature, now present in all the braces, is most valuable for the female patient. A band fashioned in this manner does not press upon the breast.

There has been little difficulty in getting the patients to wear this splint, even in cases other than fractures. Once fitted properly over an undergarment, the patient can then dress over it with a loose fitting dress, coat, or sport clothes, so that only the hand piece is visible; patients are pleased by this fact. This advantage does not apply while skeletal traction is necessary.

It has been our experience in fractures involving the upper two-thirds of the humerus, that lateral displacement of fragments is rarely a problem. Expressed in another manner, once the fragment is satisfactorily aligned in the anteroposterior roentgenogram, lateral views will show a satisfactory reduction in the great majority of cases.

Other methods of treatment for fractures of the upper end of the humerus and types of apparatus used are described in the various textbooks that concern fractures and dislocations. Many of these methods confine the patient to bed for the duration of the fracture; certain others, require the use of heavy plaster casts with incorporated devices for traction. Some, by their very nature, prohibit the use of physical therapy during the treatment. As a result, circulation is impaired. This, in turn, often may result in delayed union and limitation of neighboring joint movements.

SUMMARY AND CONCLUSIONS

1. A simplified treatment of fractures of the upper two-thirds of the humerus is described.

2. The method has been used for a long period.

3. It has been found to be a satisfactory treatment for the great majority of fractures affecting this area. An illustrative case history is reported. Ordinarily this fracture would have required open reduction but it was treated conservatively with a good end-result. Approximately 90 per cent of fractures in this area can be treated by this simple ambulatory method.

4. An abduction splint that has been redesigned many times is described. In addition to the other uses, it has been found to be helpful in the conservative treatment of certain types of fractures of the clavicle, and in the relief of the pain that accompanies incomplete ruptures of the supraspinatus tendon (subdeltoid bursitis).

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EDITORIALS

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SURGERY AND THE CANCER PROBLEM

An appeal is being made to the American public for sums aggregating several millions of dollars for a "fight against cancer." The cause is a worthy one, but distribution of money collected in its name entails considerable responsibility.

In general, cancer research has been interpreted to mean laboratory investigation with spontaneous and transplantable tumors, genetic studies, observations on the metabolism of cells *in vitro*, the chemistry of carcinogens, hormones, etc. Much basic information has been obtained concerning the nature of neoplasia; and such studies must be continued and expanded. However, unlike the situation in the fields of infectious and metabolic diseases where laboratory investigation has often afforded immediate benefit for clinical practice, cancer research has yielded comparatively little of direct benefit for the sufferer with cancer.

Great discoveries may come suddenly and from unexpected quarters; at the moment there is little indication that a biologic method for prevention and cure of cancer is imminent and there appears to be no one field that justifies intensive concentration of material resources and research effort at the expense of all other phases of the general problem.

Knowledge of cause does not assure means for control. It became possible to control the spread of small pox before the general acceptance of the germ theory of disease and long before the development of modern immunology. The specific cause of tuberculosis has been known for decades yet no specific therapy has been devised.

The endeavors of surgeons over the years to meet the challenge of cancer have resulted in appreciable advances in treatment. Six decades ago cancer of the breast was almost invariably fatal; today the patient with early cancer is offered at least a "60 per cent chance" for cure. At the turn of the century cancer of the stomach was regarded as hopeless. An interesting paper by no less an authority than the late William H. Welch, written in the eighties, four years after Billroth's first pylorectomy, included a discussion of why the surgical attack against cancer of the stomach was doomed to failure. Each one of the "insurmountable" obstacles mentioned has since been partially or completely surmounted. Today, the patient surviving five years following gastrectomy for cancer is no longer a medical curiosity. Fifteen years ago the patient with cancer of the lung, lower esophagus, proximal stomach, or pancreas was regarded as hopeless merely by

virtue of the location of the growth; today operations for removal of these neoplasms are carried out in many centers and patients have survived for years. Furthermore, improvement in cancer surgery based upon advances in supportive treatment permits appreciable extension of life in comfort for some patients belonging to a group previously regarded to be in the terminal stages of the disease. Indeed, prolonged survivals among them are increasing as time goes on. Irradiation therapy and radiobiology stem directly from an empirical clinical application of radium and x-rays to superficial neoplasms.

These endeavors must not be classified merely as phases in the routine care of patients by clinicians engaged in the routine practice of their profession. They constitute "cancer research" of a type, and no small measure of success has been attained.

The cause of cancer may be closely associated with the "cause" of living protoplasm itself and it is possible that sufficient fundamental knowledge of mechanisms of causation to enable control is still in the far future. Besides, as heretofore pointed out, knowledge of cause does not necessarily afford the means for control.

In the meantime the sufferer from cancer cannot await the future solution of the cancer problem. His situation is urgent and must be met immediately with the means at hand. With few exceptions, the only hope for cure lies with surgery, undertaken in the early stages of the disease; and for the exceptions, with irradiation, properly carried out. By continually improving the surgical and irradiation treatment progress will be made. If advances in the next 2 decades in the surgical management of cancer are comparable to those of the past 20 years, another important forward step will have been achieved which will be of direct benefit for the sufferers of this disease. Appreciation of the proper place and importance of surgery in "the fight against cancer" is necessary in any plans for an extensive project along these lines. Failure of such appreciation would tend to restrain the further development of the one method of treatment with wide application that has been increasingly successful throughout the years and which along with irradiation in selected cases may continue to be the only generally effective therapy for a long time to come.

ALEXANDER BRUNSCHWIG.

A PLEA FOR THE PERSONAL CASE RECORD

ONE of the paradoxes of the day is the degree of ignorance concerning personal health and past illnesses found in the majority of individuals. A man who knows with certainty the exact status of a bank account, income tax, social security, insurance programs, et cetera, is conversely uninformed about the state of his present health and the true history of his previous illnesses. This deficiency is apparent on a review of the medical histories related by patients on successive hospital admissions or when the details are secured independently by two or more physicians. The errors in this information held by the patient are more obviously revealed by consulting the hospital records of past admissions. For example, the average patient does not know the operative findings, the nature of complications experienced, the proper final diagnosis, and the laboratory data of any surgical procedure performed on his person.

If one were to live in the same community from birth to death and always utilize the one community hospital and remain under the all-inclusive care of one doctor during this period, the present editorial and suggestions would be

unnecessary. In this age, however, almost every adult has consulted a number of physicians for various purposes, and each doctor is confronted with the problem not only of the chief or present complaint, but the condition of the patient as a whole and the relation of the present illness to past diseases or the handicaps of a body influenced by such past diseases. He may be content with a verbal report by the patient or he may deem it sufficiently important to consult the previous hospital records. In emergencies, there may be no opportunity to secure any information whatsoever.

The possession of a written, accurate personal health record or medical diary is as valuable as any birth certificate, wedding license, genealogical tree, diploma or any other treasured document. It can be achieved only by the meticulous accumulation of such information during one's lifetime.

Such a volume could start with the hereditary factors of familial diseases and list the causes of death of near relatives. From then, in orderly sequence could be related the type of birth and incidents in child development, such as ages at teething, walking and talking and the rate of growth. The diseases of infancy and childhood would be followed by those of adolescence, adulthood and senility in year by year notation. Each visit to a physician for minor illnesses would be recorded by the physician himself in a brief paragraph stating the diagnosis and treatment.

A separate sheet in the case record book would be used for noting the dates of vaccinations, tests for immunities, injections of sera and allergic reactions. A dental form would be a corporate part of the system with the details of extractions, dental restorations and oral infections written by the dentist. All laboratory data such as urinalysis, blood counts, blood chemical studies, stool, sputum, blood typing, basal metabolic determinations would be listed on proper sheets with exact dates for future references.

In the case of females, the menstrual, gynecological, and obstetrical histories would be given in separate detail in the personal case record book. Pocket sheets for electrocardiographic tracings and miniature reproductions of roentgenograms would be integral parts of the record.

With each hospital admission the case record book is submitted by the patient and attached to the hospital chart until the day of discharge. An accurate summary of the past illnesses could be made by the interne without interrogating the patient. When patient left the hospital, a discharge note would include the exact diagnosis, the course of the disease, the complications, the surgical procedures and operative findings, if the treatment were surgical, the pathological diagnosis of any specimen removed and all laboratory and radiographic reports; this summary would be the responsibility of the attending physician.

Personal case records of the type described would be of great value to the patient and to the physician as well. They would have economic value because of the avoidance of so much unnecessary duplication of case recording. Such records would constitute an important source for statistical study if the method were commonly employed.

GEORGE T. PACK.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE author of *Plaster of Paris Technique*[1] believes that anyone with a moderate degree of manual dexterity can learn how to apply a plaster-of-Paris cast. He states correctly that the plaster cast is the best splint at the surgeon's command. It is inexpensive, durable, and is form fitting. It is a form of splint that renders itself to any specific situation.

Comparatively little has been written on the subject but the author calls especial attention to Luck's writings.

This book is written for students, house officers, and those who are called upon to treat injuries. The manuscript is well written. The illustrations are instructive. The book is divided into four sections: general considerations, the upper extremity, the lower extremity, and the vertebral column.

The author advises (1) no padding other than stockinette; (2) careful molding over bony prominences; (3) avoidance of wrinkles; (4) avoidance of adhesive beneath casts; (5) avoidance of any circular bandage other than sheet wadding under a cast; (6) application while bandage is sloppy wet; (7) no pulling during application.

He emphasizes the importance of pain, numbness, cyanosis, anesthesia, and edema as danger signals of complications. He believes it is unnecessary to split all casts immediately after application as a routine procedure.

The application of the full arm splint is well illustrated.

There are very few who would fail to enjoy and profit by reading this book. It should be in every plaster room and in every orthopedic library.

PHILIP LEWIN.

MANY new selections have been added to *The Classic Descriptions of Disease*[2] by Ralph H. Major which have definitely enhanced its value, though many a reader would doubtless wish to include still others depending on what his special interests are and who among the immortals are his favorites. One can derive much pleasure through reading the 287 selections from the original accounts of 195 authorities. These selections include a wealth of material of value to the practicing physician, teacher, and student.

The subjects chosen are divided into infectious diseases; diseases of metabolism; lead poisoning; diseases of the circulatory, blood, kidney and respiratory systems; deficiency diseases; allergic diseases and diseases of the digestive tract.

In some of these chapters perhaps more is included than is necessary; in others, one could wish for more. Obviously there is no limit to the amount of material that could be included, and the author must be congratulated on the selections he has made. This volume deserves commendation and is a worthy addition to the physician's library.

THEODORE R. VAN DELLEN.

THE medical profession is provided with an excellent coverage of world's literature in the field of radiology by offering in *The 1945 Year Book of Radiology*[3] concise but lucid abstracts of selected articles with adequate illustrations. In this the 50th anniversary year of the discovery of x-ray by Roentgen, with the world in turmoil, when the needs of the armed forces depleted the number of physicians in civilian practice to a bare minimum, it is gratifying to note the excellence and number of contributions published in the past year.

A perusal of this volume will acquaint the reader with the progress and latest achievements in diagnostic roentgenology and radiation therapy. It should stimulate him to refer to original articles for more detailed discussions. In collecting this material, the editors have selected 314 contributions from 91 clinical scientific publications of the United States and 16 other countries. The volume of 464 pages with 342 illustrations is well bound, and printed and comprehensively indexed.

Radiologists will not fail to add this volume to their library and look forward from year to year for its publication. To those physicians not familiar with the excellent content of the book, it is recommended without reservation. EARL E. BARTH.

THE manual entitled *Roentgen Diagnosis of Diseases of the Gastrointestinal Tract*[4] is the outgrowth of mimeographed outlines which the author John T. Farrell, used for some years in teaching students in radiology in the Graduate School of Medicine of the University of Pennsylvania.

The text is presented according to the "Standard Classified Nomenclature of Disease" published by the American Medical Association. Each pathologi-

[1] PLASTER OF PARIS TECHNIQUE: IN THE TREATMENT OF FRACTURES AND OTHER INJURIES. By T. B. Quigley. New York: The Macmillan Co., 1945.

[2] CLASSIC DESCRIPTIONS OF DISEASE; WITH BIOGRAPHICAL SKETCHES OF THE AUTHORS. By Ralph H. Major, M.D. 3d ed. Springfield, Illinois: Charles C Thomas, 1945.

[3] THE 1945 YEAR BOOK OF RADIOLOGY. DIAGNOSIS. Edited by Charles A. Waters, M.D., and Whitmer B. Firor, M.D. THERAPEUTICS. Edited by Ira I. Kaplan, B.Sc., M.D., Chicago: The Year Book Publishers, Inc., 1945.

[4] ROENTGEN DIAGNOSIS OF DISEASES OF THE GASTROINTESTINAL TRACT. By John T. Farrell, Jr., M.D. Springfield, Illinois: Charles C Thomas, 1946.

cal condition is described in terms of alterations in contour, motility, and position.

The topics discussed include: esophagus; stomach; small intestine; colon; appendix; rectum; anus; combined diseases of the stomach and intestine and diseases of the intestine.

The methods of examination are presented at the beginning of each topic. A summary at the conclusion of each chapter classifies the diseases according to their effect upon contour, motility, and position.

This book is recommended as an excellent guide in the examination and diagnosis of diseases of the gastrointestinal tract. R. B. LEWIS.

IN the small monograph, *Renal Tuberculosis and Roentgenologic Examination*,[1] Steinhert presents a survey and a discussion of the different diagnostic methods employed in the examination of 60 cases of surgical renal tuberculosis with special reference to the roentgenologic diagnosis. The material consists of the cases of patients with renal tuberculosis who were admitted into the Ulleval Hospital from 1938–1941. The value of excretory urography and the dangers which may attend instrumentation are discussed. An interesting and informative chapter is devoted to a discussion of renal reflux or back flow. The author advocates the application of pressure for adequate visualization of urinary tract by the excretory method. Short case histories of the 60 patients studied are found at the end of the volume. The literature, both European and American, is well covered. The illustrations are in the negative phase and depict all stages of renal tuberculosis.

The monograph—an instructive monograph deserving recommendation to urologists and roentgenologists as a valuable addition to their libraries—is translated into English with the summary translated into both French and German.

EARL E. BARTH.

IN the monograph, *Cerebral Angiography with Perabrodil*,[2] Engeset has compiled the material from 1940 to 1944 at the Neurological Department of the University Clinic of Oslo. Since thorotrast was not accepted as being absolutely harmless, 35 per cent perabrodil has been used satisfactorily as the contrast substance since 1938. Thorotrast is used only when perabrodil produces pain and for patients with mental disorders. From 6 to 20 cubic centimeters per injection and from 6 to 52 cubic centimeters per seance are used. The material covers the author's experience in performing angiographies on 100 patients with a total of 190 injections. Patients with mental disorders often react violently so thorotrast is used instead of perabrodil. Death occurred in two instances. One patient in coma was subjected to both ventriculography and angiography and expired a few hours later. The other patient, suffering from malignancy of the kidney with intracranial metastases, was subjected to angiography in the final stage of the illness. In neither instance was the cause of death ascribed to the injection of perabrodil.

In discussing the subject the author devotes sections to a historical review, to a comparison of contrast substances, to indications, contraindications, and technique; to the anatomy of the blood vessels, tumor localization, type diagnosis; to cerebral angiomas, cerebral aneurysms, cerebral arteriosclerosis and carotid thrombosis, and to therapy. The injections were all made by the neurosurgeon, Torkildsen, or his assistants. Brief case histories including a description of x-ray findings and excellent illustrations in the negative phase are used in presenting the clinical material.

The presence of several corrections is not found to be confusing. The volume is recommended to neurosurgeons, radiologists, and physicians interested in this specialized procedure.

EARL E. BARTH.

IN this excellent monograph, *The Radiosensitivity of the Bone Marrow*,[3] Denstad discusses a subject of much interest and vital importance not only to the radiologist but to all physicians who recommend the use of irradiation in the treatment of malignant and benign lesions. The work of previous investigators is adequately evaluated. The author has investigated both the indirect and the direct effect of irradiation.

The majority of the patients studied were undergoing radium and roentgen treatment for malignant tumors and lymphogranulomatosis at the Norwegian Radium Hospital. The methods of irradiation and hematological technique are discussed. The author concludes that irradiation does not generally produce any changes in the nonirradiated bone marrow. If the irradiation produces granulocytopenia, however, a minor degree of maturation inhibition is found within the myelopoiesis which is regarded as the cause of granulocytopenia, since fewer neutrophile granulocytes capable of migration are found in the bone marrow. The anaphylactic or toxic factor probably has an inhibitory effect on the myelopoiesis stimulating the erythropoiesis. The indirect irradiation effect may possibly occur more easily in patients who are debilitated or whose erythropoietic mechanism is impaired prior to treatment.

In investigating the direct effect of irradiation on bone marrow, the author found the parenchymatous cells to be very sensitive. Doses of 100 r produced slight transient changes. The erythroblasts are somewhat more sensitive than the myeloid cells and the megakaryocytes. The youngest cell forms disappear early followed by the older forms when the dosage is increased. Early inhibition of karyokinesis was noted. Complete aplasia occurs after doses of

[1] RENAL TUBERCULOSIS AND ROENTGENOLOGIC EXAMINATION. A SURVEY AND A COMPARISON BETWEEN THE EFFICIENCY OF THE DIFFERENT DIAGNOSTIC METHODS IN SIXTY CASES OF SURGICAL RENAL TUBERCULOSIS, WITH A SPECIAL VIEW TO THE ROENTGENOLOGIC DIAGNOSTIC. By Ragner Steinhert. Oslo: Grøndahl-Trykk, 1943.

[2] CEREBRAL ANGIOGRAPHY WITH PERABRODIL (CAROTIS ANGIOGRAPHY). By Arne Engeset. Oslo: Fabritius & Sønners Boktrykkeri, 1944.

[3] THE RADIOSENSITIVITY OF THE BONE MARROW. By Torfinn Denstand. Oslo: Centraltrykkeriet, 1943.

2000 to 3000 r. Regeneration occurs early after small doses but later and more incompletely after larger doses. Complete regeneration has been observed after doses of 2000 to 3000 r. Only after larger doses of 3000 r or more is regeneration less complete, particularly the quantity of cells. Complete aplasia was found 3½ years after the administration of 12,000 r. Erythroblasts regenerate first followed somewhat later by the myeloid cells. No difference in the effect of large doses of radium and x-ray was found. Irradiation produces inhibition of mitosis, a forced pathological maturation of the erythroblasts and disturbances of maturation within the myelopoiesis, all of which persist far into the period of regeneration.

This excellent monograph dealing with a subject of vital importance to any physician attending patients receiving either x-ray or roentgen therapy is highly recommended. EARL E. BARTH.

THE third edition of *Gynecologic Nursing*[1] by Crossen and Hoffert has been written to fit in with the type of texts advised by the National League of Nursing Education. Its purpose is twofold: first, to teach the principles of gynecology to nurses so they may intelligently carry out various methods of examination and treatment and, second, to teach them gynecologic nursing methods.

This book of 256 pages is replete with 194 illustrations, glossary, index, and list of reference works. The authors believe that if nurses are well grounded in the theories and principles of gynecology, they may better understand the significance of diseases of the reproductive system as they pertain both to the individual and the community.

The book is divided into two parts; the first covering anatomy, physiology, disease and treatment; the second, outlining the nursing care of the gynecologic patient. Anatomy and physiology are dealt with in a simple, concise manner, terms are defined, and often lay terms are used to clarify the text. A wealth of illustrations placed close to the subjects under discussion make for easy reference. Important names and subjects are highlighted in heavy print for easy reference to the glossary where pronunciation and definitions are given. Review questions are given at the end of each chapter.

Symptoms and their significance, history, and examination are explained from the nurses' point of view, and the names and definitions of the many types of examination and their uses in differentiating gynecologic diseases are given. The entire field of gynecology is covered in the first two-thirds of the book, the latter third being reserved for the more strictly technical nursing care of the patient. Rather detailed operative procedures are fully discussed and explained. A healthy crusading spirit is noted throughout the text for the periodic examination and early treatment of pelvic disorders.

Under the nursing care section, detailed instructions discussing nursing care are given both regarding equipment and instruments needed as well as their use during the various gynecologic procedures. Many well placed illustrations admirably clarify the text, particularly in the discussion of subjects difficult to describe.

The sociologic, public health, and industrial problems are carefully covered. This volume is an excellent adjunct to nursing education.

BYFORD HESKETT.

THE book entitled *Synopsis of Gynecology*[2] by Crossen and Crossen is based on the 9th edition of the textbook *Diseases of Women* by the same authors. These authors believe that a synopsis is particularly valuable to students who intend to do general practice and to those intending to go into specialties other than gynecology because of the mass of material they must absorb from all other fields and because it offers a well digested, time saving method of becoming acquainted with gynecological disorders. Students specializing in gynecology will have a standard text on the subject, and the synopsis will offer them a small pocket review which can be read at odd moments.

This little volume, although in small print and very concise, frequently outline in form, is nevertheless quite detailed in many respects, often giving the background and early research involved in various subjects. With some 132 illustrations and 3 color plates well placed to aid in clarifying the text, there is a wealth of material crowded into this half inch thick volume. It is written with the student viewpoint in mind.

The early chapters cover anatomy and physiology of the pelvic organs including their endocrine functions, giving the background as well as modern concepts. Examination methods, both physical and laboratory, are well covered with descriptive illustrations liberally interspersed with the text. Diagnosis is thoroughly reviewed, with the signs and symptoms and their significance in localizing particular disease entities. Under treatment a note of caution is stressed in the indiscriminate use of the endocrines. Two full chapters deal with the external and lower genital tract including such subjects as relaxations and fistulas.

Several chapters are devoted to a discussion of the uterus, and they also cover inflammations, displacements, malignant and nonmalignant tumors. Pelvic inflammatory diseases are dealt with in two separate chapters outlining etiology, pathology, diagnosis, and treatment. There is one full chapter devoted to diseases of the ovary which include cysts and tumors. Menstrual disturbances are thoroughly gone into, and methods of investigation and treatment in relation to the various age groups are given. Sterility, sterilization, contraception and

[1] GYNECOLOGIC NURSING. By Robert James Crossen, A.B., M.D., F.A.C.S., and Frances W. Hoffert, R.N., B.S. 3d ed. St. Louis: The C. V. Mosby Co., 1940.

[2] SYNOPSIS OF GYNECOLOGY. Based on the Textbook *Diseases of Women*. By Harry Sturgeon Crossen, M.D., F.A.C.S., and Robert James Crossen, M.D., F.A.C.S. 3d ed. St. Louis: The C. V. Mosby Co., 1940.

premarital examinations are explained in considerable detail. Two chapters deal with miscellaneous subjects such as menopause, allergic disturbances, leucorrhea and the relationship of other body organs to the sexual organs.

Operative gynecology is covered in detail, both abdominal and vaginal, giving indications, dangers, preoperative and postoperative care. A final chapter deals with medicolegal problems.

The specialty of gynecology is thoroughly reviewed in this book. The authors state they do not include obstetrical problems, although one believes some space should be devoted to the cause and treatment of abortions and the early complications of pregnancy because in most hospitals these patients are cared for on the gynecological service.

BYFORD HESKETT.

THE author of *Biological Actions of Sex Hormones*,[1] Harold Burrows, is a well known experimental investigator who has written extensively on the nature and effects of the sex hormones. This book was written because the author believed, "that a coordinated summary of experimental inquiries in this field might be useful."

The book is divided into six sections. Part one is concerned with the gonadotrophins or the gonad stimulating hormones. Strictly speaking, gonadotrophins are not sex hormones but their inclusion in this book seems more than justified. The function of the gonads and their production of sex hormones is dependent upon and in turn has an effect upon the gonadotrophins. Part two has to do with a general consideration of the gonadal hormones: estrogens, androgens, and progestins; comparing and contrasting their chemical structure and the nature of their effects.

Part three deals more specifically with androgens, part four with estrogens and part five with progestins. The final section is entitled "The Sex Hormones of the Adrenal Cortex" and deals with the adrenal-gonad relationships. Adrenal "virilism and feminism ' are also discussed.

There is a very complete index, both as to subject and authorities quoted. The latter serves as well for a bibliography, a method of presentation which has always seemed more sensible to the reviewer than having separate bibliographies at the end of each chapter or section of a book.

Burrows' review of the literature on each subject is exhaustive and in most portions the data is reviewed in a critical manner and the significance of the experimental work is evaluated. Only rarely does he compile the data on a subject with no attempt to evaluate its significance. One suspects these latter subjects are those with which he is less familiar or those which have been of no particular interest to him.

The book is well organized and well written but it probably will be of interest or of value to a very limited audience. The data considered are almost exclusively those obtained from laboratory animals. On most subjects little or no clinical data are included. Inferences and conclusions drawn are physiological and rarely have clinical application. On the other hand the book will be of extreme value to the laboratory worker and to the rare gynecologist or endocrinologist who attempts to keep himself informed of the basic knowledge in his particular profession.

RONALD GREENE.

THE literature of hypertension and hypertensive disease has become voluminous and its evaluation difficult for the average physician. Herndon's slim book *An Introduction to Essential Hypertension*[2] provides an excellent introduction to the subject and should facilitate critical appraisal of current and future contributions in this field. Important and recent work is reviewed and included in an extensive bibliography. The author's conclusions are conservative. Essential hypertension is viewed as a deepseated constitutional disorder affecting the whole vascular system. The etiology still appears to be unknown, and diagnosis is reached by the exclusion of other conditions. Modern study of the disease requires the skills of an internist, ophthalmologist, urologist, pathologist, and surgeon. Present treatment is merely palliative, and the disappointing results of medical care have stimulated a surgical attack of the problem. The effect of lowering the blood pressure is obviously beneficial. The most satisfactory surgical procedure, at present, seems to be bilateral section of the splanchnic nerves with lower dorsal and upper lumbar sympathetic ganglionectomy. Although an operation of this kind fails to remove the cause or alter the fundamental disturbance, it is believed worth while in certain carefully selected cases. The need and value of the patient's learning to live with a chronic condition is stressed. The author defines clearly and concisely the present status of our knowledge of an important and complex problem.

WALTER H. NADLER.

THE author of *Digitalis and Other Cardiotonic Drugs*,[3] Eli Movitt, presents a useful manual.

Although the literature on digitalis has been extensive, it has embraced a host of conflicting findings and opinions, and no attempt has been made since the appearance in 1936 of Luten's treatise, to compile the sounder elements of clinical and laboratory research under separate cover. The book is organized under eight headings: (1) digitalis folium; (2), digitalis lanata; (3), lanatoside C; (4), other cardiotonic glycosides from digitalis plants; (5), strophanthus; (6), squill; (7), other cardiotonic agents of plant origin; and (8), cardiotonic glycosides of animal origin and a cardiotonic alkaloid. Each section contains a readable and orderly account of

[1] BIOLOGICAL ACTIONS OF SEX HORMONES. By Harold Burrows, C.B.E., Ph.D., F.R.C.S. Cambridge: At the University Press, 1945.

[2] AN INTRODUCTION TO ESSENTIAL HYPERTENSION. By Richard F. Herndon, M.D., F.A.C.P. Springfield, Illinois: Charles C Thomas, 1946.

[3] DIGITALIS AND OTHER CARDIOTONIC DRUGS. By Eli Rodin Movitt, M.D. New York: Oxford University Press, 1946.

chemical structure, pharmacology and clinical application. Opinions and impressions of authoritative origin have been included with reasonable completeness and discretion on contested aspects of the subject. A few glaring errors in proofreading mar a serviceable and timely book.

EDITH B. FARNSWORTH.

IN the excellent book, *The Chemistry of Anesthesia* by Adriani[1] the author reviews the fundamental science, chemistry, and presents its significant relationship to anesthesia in an interesting and comprehendible manner.

In part I the author discusses inorganic chemistry as it applies to anesthesia. Special emphasis is placed on the chemical absorption of carbon dioxide in rebreathing appliances. The two types of mechanisms, the to-and-fro and the circle, are illustrated with simple explicit diagrams. Many practical aspects are included, such as, the temperature change during absorption of carbon dioxide, the resistance to movement of gases, and the clinical efficiency of soda lime.

Part II is devoted to the chemistry of the depressant drugs in common use for clinical anesthesia. The hydrocarbons as a group produce general anesthesia but variations in structure within this group alter potency, toxicity, or may even entirely remove physiological activity of the compound. There is a wealth of detail concerning the methods of preparation, properties, impurities, and chemical tests for ethylene and cyclopropane.

In the chapter on the alcohols one finds the basic information on changing narcotic potency, water solubility, and volatility by altering the structural formula. The chapter on ethers includes a chart showing the use of ethyl ether as the basic raw material in the manufacture of anesthetic drugs, and the wide distribution of the ethyl radical in the commonly used anesthetics. The importance of the purity of ether is stressed and tests for noxious agents and contaminants are described.

Halogenated compounds and the chemical and physical changes which occur by halogenation are discussed in detail. In the chapter on local anesthetic drugs there is a valuable table which included 20 different preparations comparing them as to chemical nature, solubility, and properties. Similar attention is given to the drugs affecting the autonomic nervous system and to the analeptics. The subject of explosions—factors influencing their production and the limits of inflammability—is treated briefly.

Part III deals with the biochemical aspects of anesthesia, i.e. the chemical changes in tissues induced by the administration of anesthetic drugs to man and animals. Animal experiments are wisely mentioned only when those on men are not available. Most theories of narcosis are based upon chemical, physical, or physicalchemical phenomena observed in cells. Each theory of narcosis is interrelated, and for this reason the entire subject is complicated. The author suggests that we may now have a few links to the still incomplete chain explaining the depression of the central nervous system. Then follows a description of the three separate compartments of body fluids—the vascular space, the interstitial fluid space, and the intracellular spaces—and the effects which anesthesia can have on the constituents of these fluids. There is also valuable information on the effects of anesthesia upon liver function, nervous tissue, and composition of urine.

Enzymes, vitamins, and hormones may play important rôles in anesthesia, and the data which exist at the present time are lucidly recorded. There is a thorough discussion of the detoxification and the elimination of anesthetic drugs.

The bibliography is especially fine in that it not only lists references according to the section of the book, but lists them according to each specific subject. It is a bibliography which can be used repeatedly. A glossary of terms, tables, and other information is also provided.

This book fills an important place in the library of the anesthesiologist. Heretofore it was necessary to search through many periodicals and books to find the material which is accumulated in this manuscript. Although it is basically for the anesthesiologist it has more than casual interest for the chemist, pharmocologist, and research worker. It is well written and well organized, and the subject becomes alive and comprehendible to the reader.

EDITH EASON and MARY KARP.

IN its second edition, *Modern Anesthetic Practice*[2] a member of *The Practitioner Handbook* series has been completely revised. Like the first, it is planned for the occasional anesthetist, rather than the specialist. The contributors include the leading English anesthetists who have arranged a manual of basic principles which will be of value to the general practitioner to whom it is addressed. The specialist, however, will also find helpful suggestions.

The introduction warns that though the advantages accruing from the increasing complexities of anesthetic apparatus are obtained at a price; the simpler methods are safer for those not specially trained.

A brief outline of the essential physiology is included and the use of volatile agents, which is the chief reliance of the occasional anesthetist, is considered in some detail.

This reviewer feels that too much emphasis is placed on the use of nitrous oxide in major surgery and that the technique described, that of secondary saturation, introduces unjustifiable hazards of anoxia. In the hands of the occasional anesthetist, this technique may be even more dangerous than its use by the specialist.

[1] THE CHEMISTRY OF ANESTHESIA. By John Adriani, M.D. Springfield, Ill.: Charles C. Thomas, 1940.

[2] MODERN ANESTHETIC PRACTICE. Edited by The Late Sir Humphry Rolleston, Bt. G.C.V.O., K.C.B., M.D., F.R.C.P., and Alan Moncrieff, M.D., F.R.C.P. 2d ed. Published on behalf of *The Practitioner*. London: Eyre and Spottiswoode Ltd., 1940.

The drugs and methods of administration of basal narcosis are described, including the administration of pentothal sodium rectally and intravenously. The discussion of endotracheal anesthesia is comprehensive.

In the chapter on spinal anesthesia it is recommended that the use of this method by the practitioner be confined to operations on the lower half of the body.

Considerable attention is given to the various phases of anesthesia and analgesia in obstetrics and it is stressed that spinal and caudal anesthesia for obstetric procedure should be reserved strictly for the specialist working under favorable conditions.

Premedication and methods of anesthesia for the child and for dental operations are discussed in detail.

Local anesthesia and refrigeration anesthesia are covered too sketchily for practical advantages. The anesthetic aspects of postoperative care are treated briefly, as are explosion hazards.

In general, the methods and apparatus described are applicable primarily to surgical practice in Great Britain and the American practitioner's interest will be largely academic. MARY FRANCIS POE.

THE volume *Medicine in Industry*[1] by Bernhard Stern is one of the series published under the auspices of the Committee on Medicine and the Changing Order of the New York Academy of Medicine. The author is a lecturer in sociology at Columbia University and Visiting Professor of Sociology, Yale University. The book has been made available by the Commonwealth Fund.

The objectives of the Committee are defined as follows:

"To explore the possibilities and to formulate methods of maintaining and improving standards of quality in medical service, including medical research, medical education, the maintenance of health, both physical and mental, the prevention of disease, and the treatment of disease.

"To study the means of making available to larger groups of people and to the country as a whole the best known practice in preventive and curative medicine.

"To explore the possibilities and to formulate proposals of distributing these services not only to a larger number but also at a lower per capita cost than the present system permits."

The author traces in broad perspectives the social, economic, legal, and professional setting within which industrial medicine has matured and the development of the scientific knowledge which has given industrial physicians increased competence to cope with diseases affected by occupations. It delineates the prevailing disastrous rates of industrial disability and the limited extent of preventive services in industry. Recent developments in health and insurance programs are appraised and the problems of the handicapped in industry outlined. The findings which emerge offer grave challenges to the public and to the profession, not merely to expand knowledge in the field of industrial medicine, but to apply more extensively the vast body of knowledge already available in the interests of the health and welfare of the nation.

The author has presented a somewhat sketchy but very thoughtful summation of the subject of industrial medicine. The general impression left by the book, is that both industrial management and the medical profession are not adequately coping with the problems presented in the field of industrial medicine and surgery. C. T. OLSON.

PUBLISHED by the Commonwealth Fund, *Nursing in Commerce and Industry*[2] by Bethel J. McGrath is truly deserving of attention by the medical profession. Mrs. McGrath has done a most excellent job of presenting a picture of the modern nurse in commerce and industry. She is a dynamic writer and has gone into every phase of her subject with extreme thoughtfulness. Each chapter is followed by an extensive bibliography. So far as I know it is the only book published giving a comprehensive view of industrial nursing and medicine.

Although this volume has been written for the industrial nursing profession, it should be required reading for all medical students before graduation and for all physicians in any way connected with industry and commerce. It has been estimated that at the present time 90 per cent of the entire medical profession does not come in contact with industry and commerce, and except for the few who specialize in this field there is a definite lack of knowledge as to the importance of this field of medicine. This volume could very easily be used as a primer for the physician entering the field of industrial medicine.

The author, a registered nurse and a very exceptional personality, has written from the viewpoint of the nurse. One might almost conclude that industrial medicine came into being and has flowered solely through the efforts of the industrial nurse. Any contributions by the medical profession are considered of very recent origin. There may be a certain amount of casuistry on the part of the author. She states that the industrial nurse is not supposed to practice medicine, but details how the industrial nurse should set up a medical department and suggests that she be subject to the authority only of someone in the top management.

In her preface the author says: "The fact that the nursing profession, management, and medicine are not agreed as to her (industrial nurse) scope and function is not strange in so broad and diversified a field."

Because of a certain amount of confusion existing as to the placing of responsibility, the author takes a definite stand by suggesting throughout her book that the nurse can be more or less all sufficient in

[1] MEDICINE IN INDUSTRY. By Bernhard J. Stern, Ph.D. New York: The Commonwealth Fund, 1940.

[2] NURSING IN COMMERCE AND INDUSTRY. By Bethel J. McGrath, R.N. New York: The Commonwealth Fund, 1940.

industrial work. There are many exceptional nurses in the industrial field and we would not argue but that some of them give far better service than do doctors. The fact that nurses are so prominent in the field of industrial medicine is due mainly to the fact that the medical profession has sadly neglected this field and that management, which is always looking for a bargain, is willing to utilize the services of a nurse in place of a medical man. American medicine is awakening to its responsibility and more and more is convincing management that all of its medical and health programs should be supervised by physicians. So far this idea has taken hold only in larger organizations, so that medical care in the majority of industries in the United States today is under the direction of nurses and part time doctors. I believe it will be definitely the attitude of the American medical profession as time goes along that all industrial medicine should be directly under the supervision of the profession and that nurses in this field should be responsible not to someone in the top lay management but to a doctor, who in turn will report to the lay management.

There is a certain amount of danger in the attitudes created by this book in that nurses may be given the impression that they can take over tasks which legally and properly belong to the medical profession and that it is not required that they have direct medical supervision. As long as the medical profession does not bestir itself to take a more active interest in industrial medicine, Mrs. McGrath's teachings are justifiable. The responsibility for the present situation rests directly upon the medical profession. C. T. Olson.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Surgical Treatment of the Nervous System. Supervising Editor Frederic W. Bancroft, A.B., M.D., F.A.C.S. Associate Editor Cobb Pilcher, M.D., F.A.C.S. Philadelphia, London, Montreal: J.B. Lippincott Co., 1946.

Modern Management in Clinical Medicine. By F. Kenneth Albrecht, M.D. Baltimore: The Williams & Wilkins Co., 1946.

The Traumatic Deformities and Disabilities of the Upper Extremity. By Arthur Steindler, M.D., F.A.C.S. In collaboration with John Louis Marxer, M.D. Springfield, Illinois: Charles C Thomas, 1946.

Motor Disorders in Nervous Diseases. By Ernst Herz, M.D., and Tracy J. Putnam, M.D. Morningside Heights: King's Crown Press, 1946.

Essentials of General Anaesthesia. By R. R. Macintosh, M.A., M.D., F.R.C.S., D.A., and Freda B. Bannister, M.A., M.D., D.A. 3d ed. Springfield, Illinois: Charles C Thomas, 1945.

Doctors East Doctors West; An American Physician's Life in China. By Edward H. Hume, M.D. New York: W. W. Norton & Co., 1946.

Diseases of the Adrenals. By Louis J. Soffer, M.D. Philadelphia: Lea & Febiger, 1946.

Evolution of Plastic Surgery. By Maxwell Maltz, B.S., M.D., Sc.D., F.I.C.S. New York: Froben Press, 1946.

Preoperative and Postoperative Treatment. Edited by Lt. Col. Robert L. Mason, M.C., A.U.S., and Harold A. Zintel, M.D. 2d ed. Philadelphia and London: W.B. Saunders Co., 1946.

Semiologia da mama; semiotécnica—diagnóstico clínico, radiográfico e histopatológico—gradação de malignidade. By Aurélio Monteiro. Rio de Janeiro: Companhia Brasileira de Artes Graficas, 1946.

Cornell Conferences on Therapy. Vol. 1. Edited by Harry Gold, M.D., David P. Barr, M.D., Eugene F. DuBois, M.D., McKeen Cattell, M.D., and Charles H. Wheeler, M.D. New York: The Macmillan Co., 1946.

Treatment of Arthritis and Rheumatism in General Practice; Particularly in Women. A Different Approach to the Problem. By Bernard Aschner, M.D. New York: Froben Press, 1946.

Scientific, Medical, and Technical Books; Published in the United States of America 1930-1944; a Selected List of Titles in Print with Annotations. Edited by R. R. Hawkins. Prepared under the direction of The National Research Council's Committee on Bibliography of American Scientific and Technical Books. Washington: 1946.

Varicose Veins of the Lower Extremity. By Anthony M. Barone, M.D. Chicago, Ill., 1945.

Exercises in Electrocardiographic Interpretation. By Louis N. Katz, A.B., M.A., M.D., F.A.C.P. 2d rev. ed. Philadelphia: Lea & Febiger, 1946.

Electrocardiography; Including an Atlas of Electrocardiograms. By Louis N. Katz, A.B., M.A., M.D., F.A.C.P. 2d rev. ed. Philadelphia: Lea & Febiger, 1946.

A History of Medicine. By Douglas Guthrie, M.D., F.R.C.S.Ed., F.R.S.E. With an Introduction by Samuel C. Harvey, M.D., F.A.C.S. Philadelphia, London, Montreal: J.B. Lippincott Co., 1946.

The Management of Fractures, Dislocations, and Sprains. By John Albert Key, B.S., M.D., and H. Earle Conwell, M.D., F.A.C.S. 4th ed. St. Louis: The C.V. Mosby Co., 1946.

The Surgical Technic of Abdominal Operations. By Julius L. Spivack, M.D., LL.D. 4th rev. ed. Springfield, Illinois: Charles C Thomas, 1946.

New Human Embryology. By Bradley M. Patten. Philadelphia: The Blakiston Company, 1946.

Medical Services by Government: Local, State and Federal. By Bernhard J. Stern, Ph. D. New York: The Commonwealth Fund, 1946.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

W. EDWARD GALLIE, Toronto, *President*
IRVIN ABELL, Louisville, *President-Elect*

Committee on Arrangements
HOWARD A. PATTERSON, *Chairman;* FRANK GLENN, *Secretary*

PROGRAM FOR THE 1946 CLINICAL CONGRESS IN NEW YORK SEPTEMBER 9 TO 13, 1946

THE thirty-second annual Clinical Congress of the American College of Surgeons will be held in New York September 9 to 13 at the Waldorf-Astoria. Had war conditions not made voluntary cancellation of meetings since 1941 advisable, this would have been the thirty-sixth Congress. Practically five years will have elapsed since the Boston meeting, which will give the September Congress the significance of a quinquennial event. It is with due appreciation of this fact, and of the epochal advances in medical science achieved during the war years, that the program is being planned.

The Fellows of greater New York are working to facilitate the utilization of the clinical resources of that great medical center as background for the series of scientific sessions and hospital conferences which will be held in the headquarters hotel. Demonstrations, clinics, and clinical group conferences will be held on each of the 5 days in selected hospitals, to supplement the panel discussions, symposia, forums, and other scientific meetings at the Waldorf-Astoria in which leaders of the surgical profession from many sections of the country will take part. Visitors of outstanding reputation in the hospital field will join with local authorities in presenting a varied, timely, and stimulating program for hospital personnel.

SIXTH NEW YORK CONGRESS

This will be the sixth time that the Clinical Congress has been held in New York. The first time was in 1912, when the old Waldorf-Astoria was the scene of the third Congress. Dr. George E. Brewer was the Chairman and Dr. Charles H. Peck the Secretary of the 1912 Committee on Arrangements. Dr. Edward Martin of Philadelphia was then President of the Clinical Congress of Surgeons of North America. More than 2,600 physicians registered, and the lack of organization for regulating the attendance at the clinics precipitated the proposal by Dr. Franklin H. Martin at the business meeting on Friday afternoon, November 15, for the creation of the college.

At the same meeting Dr. Allen B. Kanavel presented a resolution which provided that "some system of standardization of hospital equipment and hospital work should be developed, to the end that those institutions having the highest ideals may have proper recognition before the profession, and that those of inferior equipment and standards should be stimulated to raise the quality of their work. . . ." and that "the President of the Congress be authorized to appoint a committee from the profession, delegated to carry the spirit of this resolution into effect, and report at the Clinical Congress in 1913." This resolution was adopted.

Another significant event was the appointment, during an evening session given to the consideration of cancer, held in Brooklyn, of a committee that formed the nucleus of the American Society for the Control of Cancer which was organized following the Congress of Physicians and Surgeons of North America on May 22, 1913.

Thus the plans for formation of the College and for the inauguration of activities in two fields which have always been among its major concerns, hospital betterment and cancer control, were initiated at the 1912 Clinical Congress in New York, 5 years before the Congress was amalgamated with the American College of Surgeons. Later Congresses were held in New York in 1919, 1924, 1931, and 1938.

FIRST POSTWAR CONGRESS

The first postwar Clinical Congress will differ from the meetings for several years prior to the war in that a return will be made to the original custom of holding the Presidential Meeting on the opening evening, Monday, and the Convocation on the final evening, Friday, instead of combining them on the first night. There are several good reasons for the change among which is the likelihood of having several hundred surgeons, who have been received into fellowship *in absentia* during the years in which no Convocation was held, added to the number of initiates for the current year who will be present for the initiation ceremonies. Related to this is the need for relieving the pressure for hotel accommodations by distributing the attendance better throughout the week than would be possible if the Convocation were held on the opening night.

COMMITTEE ON ARRANGEMENTS

A representative Committee on Arrangements has been appointed consisting of the following members:

Howard A. Patterson, *Chairman*
Frank Glenn, *Secretary*
Frank E. Adair
Albert H. Aldridge
Thomas M. Brennan
E. Jefferson Browder
George F. Cahill
Henry W. Cave
Ralph Colp
Edward J. Donovan
Merrill N. Foote
John H. Garlock
Charles A. Gordon
George J. Heuer
J. William Hinton
George H. Humphreys
William F. MacFee
John H. Mulholland
W. Barclay Parsons
Otto C. Pickhardt
Thomas H. Russell
Raymond P. Sullivan
Howard C. Taylor, Jr.
William Crawford White
Philip D. Wilson

The Committee has been working diligently for several weeks on the meeting plans and the clinical program and there is every indication that this will be a most successful congress.

CLINICAL PROGRAM

The hospitals and medical schools of greater New York are co-operating in scheduling operative and nonoperative clinics, and group clinical conferences. Visiting surgeons will have ample opportunity to attend well arranged programs of many different kinds in several of the excellent hospitals in the area. General and special demonstrations will be held such as fractures, cancer, maternal morbidity, and end-result studies; clinicopathologic and x-ray conferences; newer diagnostic and therapeutic procedures; preoperative and postoperative supportive treatment; anesthesia; and reconditioning. The newer techniques and surgical procedures may be observed by those who are interested in them.

The medical schools will hold a series of exhibits demonstrating their work which will be on display in their affiliated hospitals. The program of each hospital will be arranged to cover subjects in general surgery, obstetrics and gynecology, fractures, orthopedic surgery, thoracic surgery, neurosurgery, genitourinary surgery, ophthalmology, and otolaryngology.

PRESIDENTIAL MEETING

On Monday evening in the Grand Ballroom the Presidential Meeting will be opened with the impressive processional of the officers, regents, and honorary guests. Welcome to the assembly will be extended by the chairman of the Committee on Arrangements, Dr. Howard. A. Patterson. Dr. W. Edward Gallie of Toronto, President of the College, will preside and will deliver the Presidential Address. An inaugural ceremony will be held for the incoming officers. Foreign guests will then be introduced.

A new feature to be included in the Presidential Meeting this year will be the first Martin Memorial Lecture. Dr. Edward D. Churchill of Boston has accepted the invitation to give this lecture. This lectureship was established upon motion of the Board of Regents at its midyear meeting on April 1, as a memorial to both Dr. Franklin H. Martin and Mrs. Martin. The founder of the College and of SURGERY, GYNECOLOGY AND OBSTETRICS was joined by his wife in making the College the beneficiary at their deaths of the Journal, together with its physical plant operated by the Surgical Publishing Company of Chicago, of which they were the owners. Doctor Martin died in 1935 and Mrs. Martin in 1945.

The Martin Memorial Lecture is to be given annually during the Clinical Congress. It will deal with a scientific subject of the author's own choosing, and it will supplant the former Annual Oration in Surgery.

CONVOCATION

It is planned this year, for various reasons, to depart from the custom of recent years of holding the Presidential Meeting and the Convocation on the same evening. The Convocation is therefore scheduled for Friday evening. An Assembly of Initiates will be held prior to the Convocation on Friday in order to instruct them in the Convocation procedure and other matters.

The Convocation will open with a processional of officers, regents, and governors. The President, Dr. Irvin Abell, will preside and will make the

opening remarks, confer the honorary fellowships, and present the candidates for fellowship. Following this ceremony, a speaker to be announced later will give the Fellowship Address.

SCIENTIFIC SESSIONS

Eminent surgeons and specialists, recognized as authorities in their fields, will address the scientific sessions, to be held on Tuesday, Wednesday, and Thursday evenings. These will be conducted as symposia, and the subjects for the three nights will be as follows: Tuesday, "Care of the Patient Before and After Operation"; Wednesday, "Venous Thrombosis and Prevention of Pulmonary Embolism"; and Thursday, "Antibiotic and Chemotherapeutic Agents in Surgery." The annual Fracture Oration will be included in the Wednesday evening program.

Single major panel discussions will be held every afternoon, from Monday through Thursday, as follows:

Monday, 1:30 to 3:00—Rehabilitation of the Surgical Patient and Early Ambulation

Monday, 3:30 to 5:00—The Treatment of Cancer of the Large Bowel

Tuesday, 1:30 to 3:00—Thiouracil in Thyroid Disease

Tuesday, 3:30 to 5:00—Recent Trends in the Management of Carcinoma of the Cervix

Wednesday, 1:30 to 3:00—Anesthesia

Wednesday, 3:30 to 5:00—Protein Metabolism in the Surgical Patient

Thursday, 1:30 to 5:00—Spinal Cord Injuries

Friday, 1:30 to 3:00—Surgery of the Stomach

Friday, 3:30 to 5:00—Surgery of the Vascular System

A symposium on fractures and other traumas will be held on Tuesday afternoon, and a symposium on cancer on Wednesday, from 2:00 to 4:00 o'clock.

Concurrent panel discussions are also planned for Friday afternoon. Subjects to be discussed are plastic surgery, thoracic surgery, urology, neurological surgery, orthopedics, and obstetrics.

OPHTHALMOLOGY AND OTORHINOLARYNGOLOGY SESSIONS

Ophthalmology panel discussions will be held Tuesday, Wednesday, and Thursday mornings at 11:00 o'clock on, respectively, "Retinal Detachment," "Glaucoma." and "Keratoplasty." On Tuesday evening at 8:00 o'clock there will be a symposium on "Orbital Reconstruction Including Prosthesis." On Thursday evening a scientific session is planned with the following as the subjects: "Recent Advances in Ophthalmology"; "Medical Treatment of Glaucoma"; and "Visual Disturbances Associated with Head Injuries."

Otorhinolaryngology panel discussions will be held Tuesday, Wednesday, and Thursday mornings at 11:00 o'clock on, respectively, "Treatment of Meniere's Disease," "Osteomyelitis of the Skull," and "Rehabilitation of War Deafness." On Tuesday evening at 8:00 o'clock there will be a symposium on "Treatment of Deafness" and on Thursday evening a symposium on "Surgery of the Nasal Accessory Sinuses."

Of interest to ophthalmologists, otorhinolaryngologists, and other surgeons will be a symposium to be held on Wednesday evening at 8:00 o'clock on "Plastic Surgery of the Head and Neck."

FORUMS ON FUNDAMENTAL SURGICAL PROBLEMS

The Forums on Fundamental Surgical Problems will be conducted on Tuesday, Wednesday, Thursday, and Friday mornings. Included in them will be brief reports of original clinical and experimental observations relating to the broad aspects of surgery and the surgical specialties. No prepared discussions of the reports are planned, but questions and comments will be invited. Especially keen interest is expected in these sessions this year because of the accumulation of the results of 5 years of work since the last Clinical Congress. Dr. Owen H. Wangensteen of Minneapolis, chairman of the committee which is planning the program, is working toward representation of as many as possible of the various university departments of surgery in this presentation of clinical and experimental research work.

The enlistment of the interest of young men who are doing original work, through the forums, is one of the most beneficial results of these sessions which are now considered to be an indispensable feature of every Clinical Congress.

HOSPITAL CONFERENCE

Dr. W. Edward Gallie, President of the College, will address the opening session of the twenty-fifth annual Hospital Standardization Conference on Monday morning at 10:00 o'clock in the Grand Ballroom, and will preside at the meeting, which will be attended by surgeons and hospital representatives. Following Dr. Gallie's résumé of the Hospital Standardization program of the College, including plans for the future, there will be reports on the progress of the 1946 Hospital Standardization survey, final results of which, including the Approved Lists of hospitals, cancer clinics, and approved hospitals for graduate training in surgery, will be announced at the end

of the year, instead of at the Clinical Congress as was the practice in former years.

The remainder of the Monday morning session will be devoted to talks by medical and hospital authorities on advances in medicine and surgery as they affect the postwar hospital, with particular consideration of their relation to the Hospital Standardization program.

The afternoon conference on Monday will be concentrated upon current problems and the outlook for the future in nursing service. The Tuesday morning conference will have as its main subject personnel management, and the Tuesday afternoon session will be centered around personnel problems in specific fields, such as dietary, laboratory, medical records, medical social service, x-ray, physical and occupational therapy, and other professional and semi-professional services. The discussions will emphasize the importance of scientific management techniques in assuring high quality service from personnel.

The Wednesday morning conference will have as its main theme the importance of assuring high standards of care to the community and all patients through providing in the general hospital facilities for all types of illness. The subject will be discussed from the standpoint of psychiatric, tuberculous, cancer, chronically ill, and convalescent patients. The Wednesday afternoon conference will center mainly around discussion of ways of improving co-operation between general hospitals and special hospitals in the care of all types of special patients.

The Thursday morning conference will revolve around the physical plant of the hospital and the importance of improvement and modernization in raising standards of care of the patient. New mechanical and technical developments will be presented. The afternoon conference will be devoted to the hospital as the health center of the community, with consideration of the effects of this concept upon hospital public relations and upon the progress of preventive medicine and public health.

An evening conference will be held at 7:00 o'clock on Tuesday. This will be devoted to discussion of the responsibilities of trustees, and members of governing boards will be especially invited to attend and to participate. A conference will be held on Wednesday evening also. This will be a round table conference on responsibilities of hospital administrators, and the preparation which is necessary to enable them to cope successfully with the wide range of administrative problems. The discussion of these problems will interest all hospital personnel.

ANNUAL MEETING OF FELLOWS

The annual meeting of the Governors and Fellows will be held on Thursday afternoon at 1:45. There will be election of officers and governors. The annual meeting affords the Fellows of the College an opportunity to hear reports of officials on the work of the organization, and to learn how it has not only raised the professional and ethical standards of surgery, but has also promoted good hospitalization and general improvement in the practice of medicine in the United States and Canada. Each Fellow has a personal part in this work and may extend the influence of the College materially in his local community. Hospital Standardization alone offers him unlimited opportunity to provide better medical care for his patients in the hospital in which he works through continuous progress in applying the principles of the Minimum Standard which insure the best care of the patient.

Every Fellow will want to attend this important meeting, at which reports will be presented on financial affairs; Hospital Standardization; Graduate Training in Surgery; Medical Motion Pictures; Public Relations; Library and Literary Research; the work of the state and provincial credentials committees, committees on applicants, and the Committee on History Reviews; Sectional Meetings, 1946; and the Department of Clinical Research, including cancer clinics, medical service in industry, the Committee on Cancer, and the Committee on Fractures and other Traumas. Dr. Abell will report on administration of the College, staff changes, and retirements, and Dr. Arthur W. Allen, Vice-Chairman of the Board of Regents will discuss "Fellowships, Obligations and Opportunities."

STATE AND PROVINCIAL EXECUTIVE, CREDENTIALS AND JUDICIARY COMMITTEES

On Wednesday morning from 9:00 to 12:00 o'clock the State and Provincial Executive, Credentials, and Judiciary committees will meet to discuss their respective activities.

MEDICAL MOTION PICTURES

The latest available films showing surgical procedures and related subjects will be shown in the medical motion picture exhibits which will be held daily. These are a much appreciated feature of the Clinical Congress. Despite the decrease in production of such films during the war period, a surprising number of new pictures are being received by the College for review.

The schedule will be so arranged as not to conflict with either the clinical program at the

hospitals or the scientific sessions. Both sound and silent, standard and color films will be shown, all of which have been approved by the Committee on Medical Motion Pictures.

TECHNICAL AND SCIENTIFIC EXHIBITION

The technical exhibit, together with the registration and clinic ticket bureaus, will be located in the Basildon Room, Jade Room, and Astor Gallery, all on the third floor of the hotel. Leading manufacturers of surgical instruments, x-ray apparatus, sterilizers, operating room lights, ligatures, dressings, hospital apparatus and supplies of all kinds, pharmaceuticals, and publishers of medical books will be represented in the exhibition. The technical exhibits will demonstrate many of the newer features learned from our experience in the war.

ADVANCE REGISTRATION

The hospitals and medical schools of New York afford accommodations for a large number of visiting surgeons. However, in order to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the meetings and also by accommodations in the hotels. It is therefore expected that surgeons who wish to attend the Congress will register in advance.

The members of the Board of Regents regret that conditions beyond their control will not permit unpaid registration at the 1946 Clinical Congress as had previously been indicated. At their midyear meeting on April 1, 1946, they voted to restore the registration fee of $5.00 for Fellows and for endorsed Junior Candidates. Non-fellows attending as invited guests of the College will pay a fee of $10.00. No fee will be required of initiates in the classes of 1942 through 1946.

To each surgeon who registers in advance a formal receipt will be issued. This is to be exchanged for a general admission card upon his registration at headquarters during the Congress. This card is not transferable and must be presented in order to obtain clinic tickets and admission to scientific sessions.

HOTEL RESERVATIONS

With the present congested hotel conditions, Fellows are urged to make early reservation at a hotel of their choice in the New York area. Should difficulty be experienced in obtaining accommodations, the College will upon request forward a special form "Application for Hotel Accommodations" which may be sent to the Housing Bureau of the American College of Surgeons, Room 1536, 233 Broadway, New York 7. The Committee on Arrangements feels that the housing situation will remain acute in New York for some time to come and in consequence recommends that all Fellows who can do so, make their own arrangements for lodgings while there. The New York Convention Bureau is co-operating by reserving as many hotel rooms as can be obtained for Clinical Congress registrants.

Following is a list of hotels:

	Minimum Rates with Bath	
	Single	Double
Allerton House, 143 East 39th Street	$2.75	
Allerton House for Women, 130 East 57th Street	3.00	
Ambassador, Park Avenue & 51st Street	6.00	
Astor, Broadway & 44th Street	3.50	$4.00
Barbizon (Women) Lexington Avenue & 63rd Street	3.50	
Barclay, 11 East 48th Street	6.00	8.00
Belmont Plaza, Lexington Avenue & 49th Street	4.00	6.00
Beverly, Lexington Avenue & 50th Street	5.00	
Biltmore, Madison Avenue & 43rd Street	5.50	7.50
Bristol, 129 West 48th Street	2.50	3.50
Capitol, 51st Street & 8th Avenue	3.00	4.50
Carlyle, Madison Avenue at 76th Street	6.00	
Chesterfield, 130 West 49th Street	2.50	4.00
Commodore, Lexington Avenue & 42nd Street	3.50	5.50
Concourse Plaza, Grand Concourse & 161st Street	3.50	5.50
Cornish Arms, 311 West 23rd Street	2.25	4.00
Delmonico, 502 Park Avenue	6.00	8.00
Essex House, 160 Central Park South	6.00	8.00
Fifth Avenue Hotel, 24 Fifth Avenue (9th Street)	4.00	6.00
Governor Clinton, 31st Street & 7th Avenue	3.30	4.40
Henry Hudson, 353 West 57th Street	2.50	3.50
Kenmore Hall, 145 East 23rd Street	2.00	3.50
Lexington, 48th Street & Lexington Avenue	4.00	6.00
Luxor Baths Hotel, 121 West 46th Street	2.25	
McAlpin, Broadway & 34th Street	3.30	4.95
Martinique, Broadway at 32nd Street	2.75	3.85
Midston House, 22 East 38th Street	3.50	4.00
New Weston, Madison Avenue & 50th	4.00	7.00
New Yorker, 34th Street & 8th Avenue	3.85	5.50
Paramount, 46th Street, West of Broadway	3.00	5.00
Park Central, 7th Avenue & 55th Street	4.00	6.00
Parkside, 18 Gramercy Park South	2.75	
Pennsylvania, 7th Avenue & 33rd Street	3.85	5.50
Piccadilly, 227 West 45th Street	3.00	5.00
Plymouth, 143 West 49th Street	2.50	3.50
President, 234 West 48th Street	2.50	4.00
Prince George, 14 East 28th Street	2.50	4.00
Roosevelt, Madison Avenue & 45th Street	4.50	6.50
Shelton, 49th Street & Lexington Avenue	3.50	5.00
Taft, 7th Avenue & 50th Street	3.00	5.00
Times Square, 43rd Street & 8th Avenue	2.25	4.00
Tudor, 304 East 42nd Street	2.50	
Victoria, 7th Avenue & 51st Street	3.00	4.50
Waldorf-Astoria, 50th Street & Park Avenue	7.00	
Warwick, 54th Street at Sixth Avenue	5.00	
Wellington, 7th Avenue & 55th Street	3.00	4.50
Woodstock, 127 West 43rd Street	3.00	5.00

CLINICAL CONGRESS PROGRAM IN BRIEF

Monday, September 9

10:00 General Assembly for Surgeons and Hospital Representatives, Grand Ballroom
1:30–3:00 Panel Discussion, Empire Room
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00 Hospital Conference, Sert Room
1:00 Surgical Film Exhibition (General), Grand Ballroom
3:00–5:00 Panel Discussion, Empire Room
8:00 Presidential Meeting, Grand Ballroom

Tuesday, September 10

9:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
10:00 Hospital Conference, Sert Room
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Jensen Suite
9:30–12:00 Forum on Fundamental Surgical Problems, Grand Ballroom
10:00 Surgical Film Exhibition (General), Empire Room
11:00 Panel Discussions
Ophthalmology
Otorhinolaryngology
1:30–3:00 Panel Discussion, Grand Ballroom
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00 Hospital Conference, Sert Room
2:00 Symposium on Fractures and Other Traumas
2:00 Surgical Film Exhibition (General), Empire Room
3:30–5:00 Panel Discussion, Grand Ballroom
7:00 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
7:00 Hospital Conference—Trustees, Sert Room
8:00 Scientific Session, General Surgery, Grand Ballroom
8:00 Scientific Session, Panel Discussion Ophthalmology, Jensen Suite
8:00 Scientific Session, Otorhinolaryngology, Le Perroquet Suite

Wednesday, September 11

8:00 Meeting of Cancer Committee, Carpenter Foyer and Dining Room
9:00 Clinics, Demonstrations and Clinical Group Conferences, Selected Local Hospitals
9:30 Hospital Conference, Sert Room
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
9:30–12:00 Forum on Fundamental Surgical Problems, Grand Ballroom
10:00 Surgical Film Exhibition (General)
State and Provincial Committees:
9:30 Judiciary Committees
10:00 Executive Committees
10:30 Credentials Committees and Committees on Applicants
} Empire Room
11:00 Panel Discussions
Ophthalmology
Otorhinolaryngology
12:00 Meeting of Board of Governors, Jensen Suite
1:30–3:00 Panel Discussion, Grand Ballroom
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00 Symposium on Cancer, Empire Room
2:00 Surgical Film Exhibition (General)
2:30 Hospital Conference, Sert Room
3:30–5:00 Panel Discussion, Grand Ballroom
6:00 Vandyck Reunion Dinner, Le Perroquet Suite
7:00 Surgical Film Exhibition Eye, Ear, Nose and Throat), Empire Room
7:30 Hospital Conference, Sert Room
8:00 Scientific Session, General Surgery, Grand Ballroom
8:00 Scientific Session (Eye, Ear, Nose and Throat), Empire Room

Thursday, September 12

9:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
9:30 Hospital Conference, Sert Room
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
9:30–12:00 Forum on Fundamental Surgical Problems, Grand Ballroom
10:00 Surgical Film Exhibition (General), Empire Room
11:00 Panel Discussions
Ophthalmology
Otorhinolaryngology
1:30 Adjourned Meeting, Governors, Grand Ballroom
1:45 Annual Meeting, Fellows, Grand Ballroom
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00 Hospital Conference, Sert Room
3:00 Panel Discussion—Graduate Training in Surgery, Jensen Suite
3:30–5:00 Panel Discussion, Grand Ballroom
3:30 Surgical Film Exhibition (General), Empire Room
3:30 National and Regional Fracture Committees, Le Perroquet Suite
4:00 Committee on the Library, Room 4-J
7:00 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
8:00 Scientific Session, General Surgery, Grand Ballroom
8:00 Scientific Session, Ophthalmology, Empire Room
8:00 Scientific Session, Otorhinolaryngology, Sert Room

Friday, September 13

9:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat), Empire Room
9:30–12:00 Forum on Fundamental Surgical Problems, Grand Ballroom
10:00 Surgical Film Exhibition (General), Empire Room
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00–4:00 Panel Discussions
Obstetrics, Sert Room
Plastic Surgery, 4-U Blue Room
Neurological Surgery, Assembly Room M-N
Thoracic Surgery, Jensen Suite
Urology, Le Perroquet Suite
Orthopedic Surgery, Carpenter Foyer and Dining Room
2:00 Surgical Film Exhibition (General), Empire Room
8:00 Convocation, Grand Ballroom